REMARKS

Claims 12-23, 25-50, 52, 53, 55, 56, 58, 59, 61-79 are pending in the application and under active consideration. Claim 24 has been canceled without prejudice or disclaimer.

A new Sequence Listing setting forth a revised sequence of SEQ ID NO:1 is filed concurrently herewith. SEQ ID NO:1 now corresponds to the sequence of native mature human IL-2 disclosed in Figure 2b of U.S. Patent No. 4,738,927, which was cited in the instant application, for example, at page 17, line 13, and incorporated by reference. The Examiner is respectfully requested to enter the Sequence Listing.

Claims 12, 16, 17, and 42 have been amended to make explicit that the recited variants of IL-2 have at least 90% sequence identity to SEQ ID NO:1. Support for the amendment can be found in the specification, for example, at page 13, lines 6-7; and page 14, lines 11-26. Accordingly, the specification provides adequate support for this amendment. Entry of the amendment is respectfully requested.

Claims 12, 16, 17, and 42 have been further amended to make explicit that the anti-HER2 antibody comprises a complementarity determining region (CDR) of an anti-HER2 antibody selected from the group consisting of 4D5 (ATCC Number CRL-10463) and 520C9 (ATCC Number HB-8696), wherein said anti-HER2 antibody binds to the extracellular domain of the HER2 receptor protein. Support for the amendment can be found in the specification, for example, at page 21, lines 23-25; page 22, line 11 through page 23, line 25; and page 29, lines 15-17. Accordingly, the specification provides adequate support for this amendment. Entry of the amendment is respectfully requested.

Claim 63 has been amended to make explicit that the humanized anti-HER2 antibody is selected from the group consisting of a humanized 4D5 antibody (ATCC Number CRL-10463) and a humanized 520C9 antibody (ATCC Number HB-8696). Support for the amendment can be found in the specification, for example, at page 22, lines 11-16. Accordingly, the specification provides adequate support for this amendment. Entry of the amendment is respectfully requested.

Claims 24, 31, 52, 55, 58, 61, 64, and 65 have been amended to include ATCC deposit numbers for the 4D5 and 520C9 antibodies. Support for the amendment can be found in the specification, for example, at page 22, lines 11-16. The ATCC numbers are reported in U.S.

Patents 5,677,171 and 6,054,561, which are cited in the text and incorporated by reference. Accordingly, the specification provides adequate support for this amendment. Entry of the amendment is respectfully requested.

Claims 12-19, 29, 32-40, 42-47, and 67 have been amended to remove fragment language. Entry of the amendments is respectfully requested.

Claims 74-79 have been amended to make explicit that the anti-HER2 antibody is Herceptin® recombinant humanized 4D5 monoclonal antibody. Support for the amendment can be found in the specification, for example, at page 29, lines 12-20. Accordingly, the specification provides adequate support for this amendment. Entry of the amendment is respectfully requested.

The present amendments do not introduce new issues, and place the subject application in condition for allowance and/or simplify issues for appeal. Accordingly, entry of the amendments after final is respectfully requested.

Cancellation and amendment of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications hereof containing the canceled or unamended claims.

Previous Amendment

The previous amendment filed September 1, 2006 was considered to be non-compliant because the text of canceled claim 60 was included in the listing of the claims. Claim 60 is currently listed as canceled without the text of the canceled claim. Applicants submit that the claim listing is now fully in compliance with 37 CFR § 1.121.

35 U.S.C. § 132(a)

The Examiner has objected to the amendment filed September 1, 2006 for allegedly introducing new matter into the disclosure. In particular, the Final Office Action alleges that the original disclosure does not provide support for the reference to SEQ ID NO:1 in the specification at page 29 and the Sequence Listing disclosing the sequence of SEQ ID NO:1, (Final Office Action, page 3).

Applicants submit that neither the Sequence Listing nor the previous amendment to the specification include new matter. As previously discussed in the response to the Office Action of March 2, 2006 the sequence of native mature human IL-2 was disclosed in Figure 2b of U.S. Patent No. 4,738,927, which was cited in the instant application, for example, at page 17, line 13, and incorporated by reference. The Examiner has acknowledged that U.S. Patent No. 4,738,927, including the sequence of SEQ ID NO:1, was properly incorporated by reference in its entirety. It was well known at the time of filing of the instant application that IL-2 is initially translated as a precursor form (Sequence 1 in Figure 2B of U.S. Patent No. 4,738,927) containing a signal peptide that is cleaved to produce the mature form starting with an N-terminal alanine (Sequence 2 in Figure 2B of U.S. Patent No. 4,738,927). See, *e.g.*, the references of Schrader et al. (1986) Proc. Natl. Acad. Sci. U.S.A. 83:2458-2462 (Fig. 1, page 2459), attached at Appendix A; and Clark et al. (1984) Proc. Natl. Acad. Sci. U.S.A. 81:2543-2547 (Fig. 1, page 2544), attached at Appendix B. **These references clearly show that Sequence 2 in Figure 2B of U.S. Patent No. 4,738,927 is the mature active form of IL-2**. The definition of IL-2 presented at page 12, lines 8-19 of the specification is clearly intended to encompass the human native mature active form of IL-2, **which was well known in the art at the time of filing**. Applicants further note that at page 29, lines 1-11 of the specification, aldesleukin is clearly described with reference to the native mature active form of IL-2.

Moreover, the specification need not recite a sequence, nor incorporate it by reference, if the sequence is known in the prior art. See, *e.g.*, *Falkner v. Inglis*, 79 USPQ2d 1001, page 1009 (Fed. Cir. 2006):

> Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. As we stated in *Capon*, "[t]he 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." *Id.* at 1358. Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential

genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences.

Applicants again emphasize that there is no requirement to describe a sequence that was known at the time of filing. Thus, the sequence of the mature form of human IL-2, which was known at the time of filing of the instant application, need not be disclosed in the application. Nevertheless, in order to expedite prosecution, the sequence of SEQ ID NO:1, which corresponds to the mature form of IL-2, is now included in the revised Sequence Listing. The sequence of SEQ ID NO:1 is disclosed in Figure 2b (Sequence 2) of U.S. Patent No. 4,738,927, **and was well known in the art to be the sequence of the mature form of IL-2**. The Examiner acknowledges that U.S. Patent No. 4,738,92 was cited and incorporated by reference in the specification at page 17, line 13. Therefore, no new matter is added by the inclusion of SEQ ID NO:1 in the revised Sequence Listing because Applicants are merely presenting a sequence that was publicly available at the time of filing. Therefore, withdrawal of the objection to the specification is respectfully requested.

Declaration

The Final Office Action alleges that a statutory bar precludes consideration of the Declaration of the inventors Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky under CFR § 1.132 because the instant application is not entitled to the priority date of U.S. provisional application 60/204,284. For the reasons discussed below, the disclosures of the instant application as well as the priority application satisfy the written description and enablement requirements under 35 U.S.C. § 112, first paragraph. Therefore, no statutory bar exists because the instant application is indeed entitled to the priority date of May 15, 2000 of U.S. provisional application 60/204,284, and the Declaration is entitled to consideration.

Priority

The Final Office Action alleges that "claims 12-50, 52, 53, 55, 56, 58, 59, 61-73, and 75-78 do not properly benefit under 35 U.S.C. § 119(e) by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as

lacking adequate written description and a sufficiently enabling disclosure" (Final Office Action, page 7). Applicants respectfully disagree.

Applicants submit that the claims, as currently amended, fully comply with the written description and enablement requirements of 35 U.S.C. § 112, first paragraph for the reasons previously made of record in the response to the Office Action of March 2, 2006, and discussed further below. Therefore, the instant application is indeed entitled to the benefit of priority of U.S. provisional application 60/204,284, filed May 15, 2000.

35 U.S.C. § 112, first paragraph, Written Description Rejection

Claims 12-50, 52, 53, 55, 56, 58, 59, 61-73, and 75-78 have been rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of an adequate written description. In maintaining the rejection, the Final Office Action alleges that only the recombinant humanized version of the murine antibody (*i.e.*, Herceptin™ (Trastuzumab)) has been shown to mediate ADCC and the murine monoclonal antibody 4D5 is ineffective (Final Office Action, page 9). The Final Office Action further alleges that "it is not by mere virtue of the epitope to which an antibody binds that the antibody has anti-proliferative effects upon cancer cells expressing HER2" (Final Office Action, page 9). The Final Office Action also alleges that the ability of the monoclonal antibody 520C9 to achieve therapeutic benefit in treating cancer overexpressing HER2 *in vivo* has not been established (Final Office Action, page 9). The Final Office Action also alleges that the genus of antibodies recited in the claims is not adequately defined:

> In this instance, there is no language that adequately describes the genus of anti-HER2 antibodies having anti-tumor activity, which when not conjugated to a cytotoxic moiety, inhibit the growth of cancer cells, so as to achieve the claimed effect. Similarly, there is no language that adequately describes the genus of biologically active variants of an IL-2 molecule comprising amino acid sequence of SEQ ID NO:1 having anti-tumor activity, which when administered in combination with the antibody inhibits the growth of cancer cells, so as to achieve the claimed effect. *A description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.*
> (Final Office Action, page 11.)

In particular, the Final Office Action alleges that claims 12, 16, 17, and 42, directed to a genus of antibodies having anti-tumor activity, which bind the same epitope as an antibody

selected from the group consisting of 4D5 and 520C9, fail to satisfy the written description requirement:

> However, as noted above, the epitope to which the antibody binds does not suffice to determine the effectiveness of the antibody to inhibit the growth of cancer cells; consequently, there is no correlation between the ability of an antibody to bind to either one of the epitopes recognized by monoclonal antibodies 4D5 or 520C9 and its ability to act effectively as an inhibitor of the growth or proliferation of breast cancer cells. Therefore, even if one were capable of recognizing or distinguishing antibodies that bind to one or the other epitope of HER2, it would still not be possible to immediately envision, recognize, or distinguish those suitable for use in practicing the claimed invention to achieve the claimed therapeutic effect. (Final Office Action, page 12.)

The Final Office Action further alleges that the skilled artisan cannot readily establish whether an antibody binds the same epitope as another antibody:

> Even using a competition binding assay, the skilled artisan cannot recognize or distinguish a ligand, e.g., an antibody that binds the same epitope as another ligand because ligands that compete with one another for binding to the same antigen do not necessarily bind the same epiotpe; rather, a ligand may bind a spatially overlapping but distinct epitope and thereby stereically hinder binding of the other ligand to its epitope. (Final Office Action, page 13.)

The Final Office Action also alleges that the specification does not teach the epitope of HER2 bound by 4D5 or 520C9; therefore, the skilled artisan would not be able to distinguish the antibodies to which the claims are directed (Final Office Action, page 13).

Applicants respectfully traverse the rejection on the following grounds.

The fundamental factual inquiry in written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. *See, e.g.*, *Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117. Determining whether the written description requirement is satisfied is a question of fact and the burden is on the Examiner to provide evidence as to why a skilled artisan would not have recognized that the applicant was in possession of claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim,* 191 USPQ 90 (CCPA 1976). It is not necessary that the application describe the claimed invention *in ipsis verba.* Rather, all that is required is that the specification reasonably

convey possession of the invention. *See, e.g., In re Lukach,* 169 USPQ 795, 796 (CCPA 1971). Finally, determining whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange,* 209 USPQ 288 (CCPA 1981).

Furthermore, the Patent Office's own guidelines on written description are clear -- the written description requirement is highly fact-dependent and there is a strong presumption that an adequate written description of the claimed invention is present at the time of filing:

> [t]he description need only describe in detail that which is new or not conventional. This is equally true whether the claimed invention is a product or a process. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics. ... A "representative number of species" means that the species that are adequately described are representative of the entire genus. ... What constitutes a "representative number" is an inverse function of the skill and knowledge of the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. ... Description of a representative number of species does not require the description be of such specificity that it would provide individual support for each species that the genus embraces. (Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099, emphasis added).

Simply put, there is absolutely **no** requirement that Applicants exemplify (or reduce to practice) every anti-HER2 antibody and IL-2 variant falling within the scope of the claims in order to adequately describe the methods of treating breast cancer as claimed. Rather, the test is whether the specification contains sufficient disclosure regarding structural and functional characteristics of the anti-HER2 antibodies and IL-2 variants to satisfy the written description requirement.

The pending claims are directed to methods of treating a subject for breast cancer characterized by overexpression of the HER2 receptor protein, comprising concurrent therapy with IL-2 and an anti-HER2 antibody that has anti-tumor activity and comprises a

complementarity determining region (CDR) of an anti-HER2 antibody selected from the group consisting of 4D5 (ATCC Number CRL-10463) and 520C9 (ATCC Number HB-8696), wherein the anti-HER2 antibody binds to the extracellular domain of the HER2 receptor protein.

The specification as filed fully describes such anti-HER2 antibodies. Representative examples of anti-HER2 antibodies are described in the specification, for example, at page 22, line 11 through page 23, line 25. Humanized antibodies, in particular, are described in the specification, for example, at page 24, line 27 through page 25, line 10. The 4D5 and 520C9 antibodies are commercially available from the American Type Culture Collection and Genentech. In addition, the nucleotide and amino acid sequences for the variable heavy and light domains of the 4D5 and 520C9 antibodies were well known in the art at the time of the present invention. See for example, U.S. Patent No. 6,054,561, disclosing these sequences for the 520C9 antibody and Carter et al (1992) Proc. Natl. Acad. Sci. USA 89:4285-4289 at Fig. 1 on p. 4286 for the corresponding sequences for the 4D5 antibody. Furthermore, anti-HER2 antibodies comprising CDR residues of a 4D5 or 520C9 antibody can readily be identified by routine methods of sequencing, and anti-tumor activity of such antibodies can readily be measured as described in the specification, for example, at page 34, line 24 through page 35, line 18. Thus, the specification contains sufficient disclosure regarding structural and functional characteristics of the recited anti-HER2 antibodies to satisfy the written description requirement.

The Examiner acknowledges that anti-HER2 antibodies with the specificity of the 4D5 antibody have been found to be effective in inhibiting the growth of cancer cells, but alleges that the efficacy of the 520C9 antibody has not been established (see Final Office Action, page 8). Applicants previously submitted the reference of Stockmeyer et al. (J. Immunol. (2003) 171:5124-5129) to provide evidence that the unconjugated 520C9 antibody has been found to induce antibody-dependent apoptosis of human breast cancer cells.

Moreover, there is no requirement that the anti-HER2 antibodies mediate ADCC as the Examiner maintains (see Final Office Action, page 9). The anti-HER2 antibodies as recited in the claims are merely required to have "anti-tumor activity" irrespective of their mechanism of action. Applicants need not prove whether anti-tumor activity is mediated through complement or ADCC cytotoxicity or by antagonizing HER2 receptor signaling by blocking the receptor ligand binding site, or some other mechanism.

Furthermore, variants of IL-2 were well-known in the art and adequately described in the specification. Given the sequence of IL-2 (*i.e.*, SEQ ID NO:1), one could readily identify variants having 90% amino acid identity by routine methods of sequence alignment (see the specification, for example, at page 14, line 21 through page 16, line 6). The art also provides substantial guidance regarding the preparation and use of IL-2 variants, and numerous representative examples of biologically active variant IL-2 polypeptides (see specification, for example, at page 16, line 26 through page 17, line 27). Accordingly, the representative number of species disclosed in the specification and art more than adequately conveys to the skilled artisan that Applicants were in possession of the variant IL-2 polypeptides at the time the application was filed.

The Examiner asserts that "[a] description of what a material does, rather than of what it is, does not suffice to describe the claimed invention" (Final Office Action, page 9). However, the variants of IL-2 described herein are characterized in the specification in terms of their sequence (structure) as well as their biological activity. Thus, the claimed variants are not defined only in terms of what they do. Similarly, the anti-HER2 antibodies are described in terms of their antigen binding domains (CDRs), their antigen specificity and their biological activity. Again, the specification teaches what the claimed anti-HER2 antibodies are, rather than simply what they do.

For at least the above reasons, withdrawal of the written description rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

35 U.S.C. § 112, first paragraph, Enablement

Claims 12-50, 52, 53, 55, 56, 58, 59, 61-73, and 75-78 have been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not provide an enabling disclosure commensurate in scope with the claims. In maintaining the rejection, the Final Office Action alleges that "the specification, while being enabling for using a method for treating a patient diagnosed with breast cancer that overexpresses HER2 comprising administering to the patient a therapeutically effective amount of Herceptin™ (trastuzumab) or an immunotoxin comprised of a humanized version of murine antibody 4D5, murine antibody 520C9, or another anti-HER2 antibody, as taught by the prior art, in combination with a therapeutically effective

amount of naturally occurring human IL-2, Proleukin™ (aldesleukin), or another recombinant human 'IL-2' molecule effective to stimulate non-specific immune response in humans, as taught by the prior art, does not reasonably provide enablement for using a method for treating a subject having breast cancer that is characterized by overexpression of HER2 according to the claims" (Final Office Action, page 15). In particular, the Final Office Action alleges that "the skilled artisan cannot reliably and accurately predict which antibodies that bind the extracellular domain of HER2 ameliorate or aggravate disease symptoms in a subject afflicted with cancer, since it is not possible to predict which of such antibodies will inhibit or enhance the growth of cancer cells, and which will have no effect" (Final Office Action, pages 16-17). The Final Office Action further alleges that "it is not by mere virtue of the epitope to which an antibody binds that the antibody has anti-proliferative effects upon cancer cells expressing HER2 (Final Office Action, page 17).

The Final Office Action also alleges that non-humanized antibodies may not be effective:

> For these reasons, it is submitted that murine anti-HER2 antibodies, including mouse monoclonal antibody 4D5 or any other non-human antibody that binds the same epitope, should not generally be regarded as suitable for use in the practice of the claimed invention, since most murine antibodies lack the ability to mediate ADCC in humans and are therefore not therapeutically equivalent to Herceptin™.
> (Final Office Action, page 18.)

In addition the Final Office Action alleges "even though monoclonal antibody 520C9 is capable of mediating ADCC, its use in practicing the claimed invention to achieve the claimed therapeutic effect in patients afflicted with breast cancer has not been exemplified or otherwise demonstrated" (Final Office Action, pages 18-19).

The Final Office Action also alleges that antibodies shown to have anti-tumor activity *in vitro* do not necessarily have anti-tumor activity *in vivo* (Final Office Action, page 19-21).

The Final Office Action also alleges that the skilled artisan could not make the antibodies to which the claims are directed without undue and/or unreasonable experimentation because the epitopes to which the antibodies bind have not been described (Final Office Action, page 23).

The Final Office Action also alleges that undue experimentation would be required to identify biologically active variants of IL-2 which could be used effectively *in vivo* to reduce tumor growth and/or tumor burden (Final Office Action, page 23).

Applicants respectfully traverse the rejection.

Applicants respectfully submit that the current claims indeed comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. In particular, claims 12, 16, 17, and 42 have been amended to make explicit that the methods use an anti-HER2 antibody that has anti-tumor activity and comprises a complementarity determining region (CDR) of an anti-HER2 antibody selected from the group consisting of 4D5 (ATCC Number CRL-10463) and 520C9 (ATCC Number HB-8696), wherein the anti-HER2 antibody binds to the extracellular domain of the HER2 receptor protein. The Examiner has acknowledged that the claimed methods for treating breast cancer comprising administering IL-2 and Herceptin® or an immunotoxin comprised of a humanized 4D5 or 520C9 anti-HER2 antibody are enabled (see, *e.g.*, Final Office Action, page 15).

The specification as filed fully describes how to make and use the recited anti-HER2 antibodies. Representative examples of anti-HER2 antibodies for use in the claimed methods are described in the specification, for example, at page 22, line 11 through page 23, line 25. The murine 4D5 and 520C9 antibodies are also commercially available from the American Type Culture Collection and a humanized 4D5 antibody is available as Herceptin® from Genentech. In addition, the nucleotide and amino acid sequences for the variable heavy and light domains of the 4D5 and 520C9 antibodies were well known in the art at the time of the present invention. See for example, U.S. Patent No. 6,054,561, disclosing these sequences for the 520C9 antibody and Carter et al (1992) Proc. Natl. Acad. Sci. USA 89:4285-4289 at Fig. 1 on p. 4286 for the corresponding sequences for the 4D5 antibody. Methods of making chimeric and humanized forms of the 4D5 and 520C9 antibodies are well-known in the art and described in the specification, for example, at page 22, line 17 through page 25, line 10. Anti-HER2 antibodies comprising CDR residues of a 4D5 or 520C9 antibody, as recited in the claims, can also readily be identified by routine methods of sequencing. The specification also describes methods of measuring anti-tumor activity of such antibodies (*e.g.*, page 34, line 24 through page 35, line 18).

The specification also describes how to make and use IL-2 variants (see specification, for example, at pages 12-21). Given the sequence of human IL-2 (*i.e.*, SEQ ID NO:1), one could readily identify variants having 90% amino acid identity by routine methods of sequence alignment (see the specification, for example, at page 14, line 21 through page 16, line 6). The

art also provides substantial guidance regarding the preparation and use of IL-2 variants, and numerous representative examples of biologically active variant IL-2 polypeptides having anti-tumor activity (see specification, for example, at page 16, line 26 through page 17, line 27). It was well known in the art at the time the application was filed that IL-2 or biologically active variants thereof had anti-tumor activity. See specification, *e.g.*, at page 3, lines 4-11 and page 17, lines 15-27, and the references cited therein.

Furthermore, the specification discloses working examples for treatment of breast cancer with Proleukin® and Herceptin® according to the claimed methods (see, *e.g*, clinical study on treatment of breast cancer patients described in the specification at Example 1). Thus, the claims are adequately enabled by the specification.

The Examiner has cited various references (Stancovski et al., Lewis et al., Keler et al., Masui et al., Kim et al., and Vuist et al.) to suggest that it is unpredictable whether an antibody that binds the extracellular domain of HER2 will "ameliorate or aggravate disease symptoms in a subject" and that *in vitro* results may not be predictive of *in vivo* therapeutic efficacy (see Final Office Action, pages 16-19).

With regard to Stancovski et al., the majority of their antibodies (*i.e.*, 4 out of 5) directed against the extracellular domain of HER2 inhibited tumor growth. Differences in behavior of the antibodies were attributed by Stancovski to epitope specificity:

> These differential biological activities can be attributed to different epitopes on the exoplasmic portion of the receptor. (page 8694)

In the instant application, the current claims recite that the anti-HER2 antibodies comprise a CDR region, that is, the antigen binding region of a 4D5 or 520C9 antibody. Antibodies containing antigen-binding residues from the CDR regions of the 4D5 and 520C9 antibodies have been shown to inhibit tumor growth. The failure to show efficacy with antibodies not containing CDR residues of 4D5 or 520C9 is irrelevant to the claimed invention. Furthermore, the claims require that the antibodies have anti-tumor activity. Thus, inoperative species, *i.e.*, antibodies that do not have anti-tumor activity are excluded by the claims.

The Examiner misrepresents the teachings of Lewis et al. as suggesting that the murine monoclonal antibody 4D5 does not show efficacy. On the contrary, Lewis shows that the murine

monoclonal antibody 4D5 was the "most potent" monoclonal antibody in inhibiting growth of breast tumor cell lines (see, *e.g.*, Abstract). Applicants emphasize that anti-tumor activity is defined in the specification in terms of inhibition of tumor growth (see specification, *e.g.*, page 6, lines 25-31), irrespective of the mechanism of action. Applicants need not prove whether anti-tumor activity is mediated through complement or ADCC cytotoxicity or by antagonizing HER2 receptor signaling. Furthermore, the failure to demonstrate efficacy in colon and gastric adenocarcinomas is irrelevant to the claimed invention, because the current claims are limited to breast cancer. Lewis demonstrates efficacy of the murine 4D5 monoclonal antibody as well as humanized and chimeric forms of the 4D5 antibody for treating breast cancer.

The Examiner cites Keler et al. as showing that a Fab fragment of 520C9 was not as effective at mediating ADCC as the bispecific antibody MDX-H210. However, Keler does not state that the 520C9 antibody does not mediate ADCC. Rather, Keler shows that coupling the 520C9 Fab to a second Fab H22 that binds to FcγRI enhances ADCC. The fact that the anti-tumor activity of the 520C9 antibody may be enhanced in various ways, such as by conjugation to an immunotoxin or second antibody fragment that targets apoptosis machinery in the cell, is not relevant to the claimed invention.

Applicants previously submitted the reference of Stockmeyer et al. (J. Immunol. (2003) 171:5124-5129) on September 1, 2006 to provide evidence that the unconjugated 520C9 antibody indeed induces antibody-dependent apoptosis of human breast cancer SK-BR-3 cells. Stockmeyer also showed that though the full 520C9 antibody induced apoptosis, the F(ab')2 of 520C9 was not effective at mediating ADCC, (see page 5126, col.2). Thus, an intact antibody comprising an Fc domain as expected would be more effective in mediating ADCC than a Fab fragment. However, a Fab fragment may inhibit tumor growth through other mechanisms, such as by effectively blocking the ligand binding site of the HER2 receptor to antagonize growth signaling, which was not tested by Keler. Applicants again emphasize that the claims are currently limited to operative embodiments, that is, anti-HER2 antibodies having anti-tumor activity, **and are not limited to only those anti-HER2 antibodies with anti-tumor activity which is mediated by ATCC.**

The Examiner cites Masui for teaching that anti-EGFR antibodies mediate anti-tumor effects by different mechanisms that are partially determined by the different isotypes of the

antibodies. Masui indicates that anti-tumor activity may result through a variety of mechanisms, including by antibodies blocking ligand binding, activation of a receptor, or otherwise perturbing receptor function, or by immune-related mechanisms, such as antibody-dependent cellular cytotoxicity or complement-dependent cytolysis. Thus, different anti-HER2 antibodies may exert anti-tumor effects in different ways. However, the claims merely require that the anti-HER2 antibodies have anti-tumor activity regardless of mechanism. The fact that many mechanisms exist by which an antibody may have anti-tumor activity does not render the claims unpatentable.

The Examiner cites Kim as suggesting that *in vivo* efficacy is not necessarily predicted from *in vitro* studies. Like Masui, Kim points out that anti-tumor activity is determined by multiple underlying mechanisms that depend not only on epitope specificity, but also on immune activation through the Fc receptor, which can be affected by antibody isotype. However, Kim does not show that *in vitro* studies are completely ineffective at predicting therapeutic efficacy, only that *in vitro* studies may not simulate all the factors present *in vivo*. Contrary to the Examiner's assertions, *in vitro* results were fairly predictive of *in vivo* efficacy in Kim's studies. The HRT antibodies showed superior anti-tumor activities to the HRO antibodies both *in vitro* and *in vivo*. All of the HRT antibodies showed anti-tumor activity *in vivo* regardless of isotype, and the IgG2b isotype, which showed the highest cytotoxicity in antibody-dependent cellular cytotoxicity and complement-mediated killing of SK-BR3 cells *in vitro*, also showed the best inhibition of tumor growth *in vivo* (see page 432, col. 1). Admittedly, not all of the HRO antibodies, which showed lower cytotoxicities *in vitro* than the HRT antibodies, albeit some cytotoxicity, were found to effectively inhibit tumor growth *in vivo*. However for the Examiner to assert that *in vitro* studies are completely unreliable on this basis is unreasonable.

The Examiner also cites Vuist as allegedly showing the unpredictability in treating cancer cells with antibodies. Applicants respectfully disagree with the Examiner's interpretation of Vuist's teachings. On the contrary, Vuist shows that IL-2 is effective in enhancing anti-tumor activities of some antibodies by inducing ADCC. In the instant application, the claimed method of treating breast cancer comprises administering IL-2 in combination with an anti-HER2 antibody. The fact that the combination of an anti-HER2 antibody and IL-2 is more effective in treating breast cancer than either agent alone is the whole point of using combination therapy.

The Final Office Action also alleges that only methods of treating breast cancer using Herceptin® and Proleukin® for which Applicants provided clinical data are enabled. However, it is improper for the Examiner to attempt to limit the claims to only those methods disclosed in specific experimental examples. An applicant need not perform an actual reduction to practice, nor describe all actual embodiments. See, *e.g.*, MPEP §§ 2164.02, 2164.03. Furthermore, applicants are not required to limit the claims only to preferred embodiments. See, *e.g.*, *In re Goffe*, 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976); MPEP §2164.08.

The Examiner acknowledges that it is "routine to screen anti-HER2 antibodies that bind the extracellular domain of HER2 to identify those that are capable of inhibiting the growth of breast cancer cells characterized by the overexpression of HER2" (see Final Office Action, page 22). Further, it is well settled that time-consuming or expensive experimentation is **not** undue if it is routine. (See, *e.g.*, PTO Training Manual on Enablement, pages 30-31, citing *United States v. Telectonics Inc.*, USPQ2d 1217, 1223 (Fed. Cir. 1988), *cert. denied* 490 U.S. 1046 (1989) holding the disclosure of a single exemplified embodiment and a method to determine other embodiments was enabling, even in the face of evidence that determining additional embodiments might require 6-12 months of effort and cost over $50,000). Thus, the possibility of generating inoperative embodiments, allegedly established by the cited references discussed above, is not relevant to the claimed invention.

Furthermore, the presence of inoperative embodiments does not necessarily render a claim nonenabled. *See, e.g.*, MPEP § 2164.08(b); and *In re Angstadt,* 537 F.2d 498, 504, 190 USPQ 214, 219, CCPA 1976. The test of enablement is not what is predictable *a priori*, but what the specification teaches the skilled practitioner in regard to the claimed subject matter. Thus, not every species (or even a majority of species) encompassed by the claims, even in an unpredictable area like the chemical sciences, needs to be disclosed. *In re Angstadt,* 537 F.2d 498, 504, 190 USPQ 214, 219, CCPA 1976. The notion that one of ordinary skill in the art must have reasonable assurances of obtaining positive results on every occasion has been emphatically rejected. *Angstadt* at 219. So long as it is clear that some species render the claims operative, the inclusion of possible inoperative species cannot invalidate the claim under paragraph 1 of 35 U.S.C. §112. *See, also, In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, CCPA 1971; *Horton v. Stevens*, 7 USPQ2d 1245, 1247, Fed. Cir. 1988.

The Examiner asserts that the rejection is proper because:

> Accordingly if by no other means, the biologically active variants of the IL-2 molecule comprising SEQ ID NO:1 to which the claims are directed would have to be made and then selected upon the basis of very complicated in vivo experiments designed to determine whether the molecules could be used effectively to cause a reduction in tumor growth and/or tumor burden. Inasmuch, as this is the very intent for which the claimed invention is to be practiced, it is submitted the claimed invention cannot be used without undue and unreasonable experimentation, as it would require the practioner to first elaborate a means for practicing the invention to achieve the therapeutic effect (see page 23).

Applicants respectfully disagree. Applicants have supplied the practitioner with a detailed description, including the sequence, of the IL-2 or variant thereof to be used in practicing the invention. Applicants have supplied the practitioner with the required regions of the anti-HER2 antibodies (whose sequences are well known in the art). Applicants have supplied the practitioner with therapeutic dose ranges of both the antibody and the IL-2 or variant thereof. It is well known in the art how to test potential therapeutics for reducing tumor growth and/or tumor burden. Applicants have supplied the practitioner with the methods used in Example 1 for testing this concurrent therapy clinically. Thus, in contrast to Examiner's statement regarding undue experimentation, these methods are routine and known in the art, and the instant specification is sufficient to enable the skilled practitioner.

For at least these reasons, withdrawal of the enablement rejection under U.S.C. § 112, first paragraph is respectfully requested.

Availability of 4D5 and 520C9 Antibodies

In addition, the rejection of claims 12-50, 52, 53, 55, 56, 58, 59, and 61-73 under 35 U.S.C. § 112, first paragraph, is maintained allegedly because Applicant has not provided the required assurance that the hybridoma cell lines, which produce the antibodies to which the claims refer have been deposited according to the provisions of the Budapest Treaty. In particular, the Final Office Action alleges that the availability of the antibodies from the ATCC is negated by the ATCC disclaimer, which states that "ATCC products are intended for laboratory research purposes only" and "are not intended for use in humans" (Final Office

Action, page 25). The Final Office Action further alleges that Applicants have not shown that the antibodies to which the claims are directed are available (Final Office Action, page 26). The Office invites applicants to deposit the hybridomas in order to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph.

However, applicants reiterate that no deposit is necessary.

MPEP §2404.01 states:

> In an application where the invention required access to specific biological material, an applicant could show that the biological material is accessible because it is known and readily available to the public. The concepts of "known and readily available" are considered to reflect a level of public accessibility to a necessary component of an invention disclosure that is consistent with an ability to make and use the invention. To avoid the need for a deposit on this basis, the biological material must be both known and readily available - neither concept alone is sufficient. A material may be known in the sense that its existence has been published, but is not available to those who wish to obtain that particular known biological material. Likewise, a biological material may be available in the sense that those having possession of it would make it available upon request, but no one has been informed of its existence.

As discussed previously in the responses to the Office Actions of February 18, 2005 and March 2, 2006, the 4D5 and 520C9 antibodies are **both** known and readily available to the public as required by MPEP §2404.01. The 4D5 (ATCC No. CRL-10463) and 520C9 (ATCC No. HB-8696) hybridomas are commercially available to the public from the American Type Culture Collection. According to the ATCC catalog available as of April 18, 2006, the 4D5 (CRL-10463) and the 520C9 hybridomas are available each for the purchase price of $330.00. The ATCC catalog is analogous to any other chemical catalog that lists materials for purchase.

The Examiner's position that the ATTC product disclaimer makes these antibodies unusable is untenable. A general product disclaimer appears in the ATCC catalog that apparently applies to all commercially available ATCC hybridoma cell lines (see Appendix C). This disclaimer is obviously intended to legally protect the ATCC from liability. However, the antibodies are clearly commercially available from the ATCC and could be readily formulated for human use by one of skill in the art and used

in the claimed methods. Therefore, the claimed subject matter is enabled. The job of the Patent Office is to determine enablement. It is not the business of the Patent Office to enforce the legal restrictions imposed by the ATCC. Furthermore, Herceptin®, a humanized form of the 4D5 antibody, is formulated for human use and commercially available from Genentech. Thus, the requirements that the antibodies be known and readily available are satisfied. In addition, the nucleotide and amino acid sequences for the variable heavy and light domains of the 4D5 and 520C9 antibodies were well known in the art at the time of the present invention. See for example, U.S. Patent No. 6,054,561, disclosing these sequences for the 520C9 antibody and Carter et al (1992) Proc. Natl. Acad. Sci. USA 89:4285-4289 at Fig. 1 on p. 4286 for the corresponding sequences for the 4D5 antibody.

For at least the above reasons, withdrawal of the enablement rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

35 U.S.C. § 102

Claims 12-15, 17, 22-26, 35-37, 52, 58, 63, 64, 66, 68, 73, 75, and 77 have been rejected under 35 U.S.C. §102(b) as being anticipated by, Fleming et al. (Abstract No. 710, Program Proceedings, American Society of Clinical Oncology, 35th Annual Meeting, 1999; hereinafter "Fleming") as evidenced by Fleming et al. (Clin. Cancer Res. (2002) 8:3718-3727). Fleming is cited for teaching a method of administering to patients a recombinant anti-HER2 monoclonal antibody in combination with IL-2 according to a dosage regimen, including IL-2 at a dose of 1.25 MIU/m^2 adminstered subcutaneously on a daily basis with intermediate-dose pulses of 15 MIU/m^2/day for 3 days every two weeks and anti-HER2 antibody at doses of 1, 2, and 4 mg/kg. Fleming also teaches reducing the dose of IL-2 to 1 MIU/m^2 daily with 12 MIU/m^2 pulses. Applicants respectfully traverse the rejection.

Claims 12-23, 25-50, 52, 53, 55, 56, 58, 59, and 61-78 are fully described in the specification of the instant application and thus are fully enabled. Applicants submit that the claims as currently amended are indeed entitled to the priority date of the U.S. provisional application 60/204,284, filed May 15, 2000, as discussed above. Therefore, the priority date of the instant application is within one year of the ASCO 1999 meeting at which the Fleming et al.

abstract was presented and subsequently published (see information on the ASCO 1999 meeting previously submitted in the response to the Office Action of March 2, 2006), and no statutory bar prevents the consideration of the previously submitted Declaration of the inventors Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky under CFR § 1.132. The Declaration states that the inventors of the present application, Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, are coauthors on the Fleming et al. ASCO abstract and the relevant portions of Fleming et al. describe applicants' own work. The remaining co-authors on the abstract are not inventors of the claimed invention. Thus, pursuant to *In re Katz*, this basis for rejection has been overcome.

35 U.S.C. § 103

A. Fleming in view of Meropol

Claims 27-31, 53, and 59 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Fleming et al. (Abstract No. 710, Program Proceedings, American Society of Clinical Oncology, 35th Annual Meeting, 1999) as evidenced by Fleming et al. (Clin. Cancer Res. (2002) 8:3718-3727) in view of Meropol et al. (Cancer Immunology & Immunotherapy (1998) 46:318-326). Applicants respectfully traverse the rejection.

As discussed above, the currently claimed invention is indeed entitled to the priority date of the U.S. provisional application 60/204,284, filed May 15, 2000; therefore, the Declaration of the inventors Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky under CFR § 1.132 is not prevented by a statutory bar from consideration. The inventors of the present application, Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, are coauthors on the Fleming et al. ASCO abstract. The relevant portions of Fleming et al. describe applicants' own work, and the remaining co-authors on the abstract are not inventors of the subject claims (see Declaration of Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, pursuant to *In re Katz*, previously submitted on September 1, 2006).

The secondary reference of Meropol fails to describe or suggest any method of treating cancer using an anti-HER2 antibody, let alone, any method of concurrent therapy using a combination of an anti-HER2 antibody and IL-2. Meropol does not suggest any specific anti-HER2 antibodies or specify which epitopes on the HER2 antigen these antibodies should bind to.

The combination of Fleming and Meropol is thus just an invitation to experiment. Therefore, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

B. Fleming in view of U.S. Patent No. 4,863,726

Claims 27-31, 53, 59, and 65 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Fleming et al. (Abstract No. 710, Program Proceedings, American Society of Clinical Oncology, 35th Annual Meeting, 1999) as evidenced by Fleming et al. (Clin. Cancer Res. (2002) 8:3718-3727) in view of U.S. Patent No. 4,863,726. Applicants respectfully traverse the rejection.

Applicants reiterate that the Declaration of the inventors Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky under CFR § 1.132 is entitled to consideration. The inventors of the present application, Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, are coauthors on the Fleming et al. ASCO abstract. The relevant portions of Fleming et al. describe applicants' own work, and the remaining co-authors on the abstract are not inventors of the subject claims (see Declaration of Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, pursuant to *In re Katz*, previously submitted on September 1, 2006).

The secondary reference of U.S. Patent No. 4,863,726 fails to describe or suggest any method of treating cancer using concurrent therapy with a combination of an anti-HER2 antibody and IL-2 administered according the claimed dosing regimens. Rather, U.S. Patent No. 4,863,726 teaches using an effective amount of a mammalian IL-2 and an immunotoxin. Combining Fleming with U.S. Patent No. 4,863,726 would lead the skilled practitioner to use a combination of IL-2 and an immunnotoxin, not IL-2 or a variant thereof and an anti-HER2 antibody comprising the CDR region of a 4D5 or 520C9 antibody, as taught in the instant application. Therefore, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

C. Fleming in view of U.S. Patent Application Publication No. 2003/0185796 A1

Claims 16, 32-34, 55, 56, and 67 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Fleming et al. (Abstract No. 710, Program Proceedings, American Society of Clinical Oncology, 35th Annual Meeting, 1999) as evidenced by Fleming et al. (Clin. Cancer

Res. (2002) 8:3718-3727) in view of U.S. Patent Publication No. 2003/0185796. Applicants respectfully traverse the rejection.

Applicants reiterate that the Declaration of the inventors Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky under CFR § 1.132 is entitled to consideration. The inventors of the present application, Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, are coauthors on the Fleming et al. ASCO abstract. The relevant portions of Fleming et al. describe applicants' own work, and the remaining co-authors on the abstract are not inventors of the subject claims (see Declaration of Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, pursuant to *In re Katz*, previously submitted on September 1, 2006).

The secondary reference of U.S. Patent Publication No. 2003/0185796 fails to describe or suggest any method of treating cancer using concurrent therapy with a combination of an anti-HER2 antibody and IL-2. Rather, U.S. Patent Publication No. 2003/0185796 pertains to methods of treating non-hodgkin's lymphoma with anti-CD20 antibodies. No mention is made of anti-HER2 antibodies. Combining Fleming with U.S. Patent Publication No. 2003/0185796 would lead the practitioner to a dosing regime comprising IL-2 and an anti-CD20 antibody, not to a combination of IL-2 or a variant thereof and an anti-HER2 antibody comprising the CDR regions of 4D5 or 520C9, as taught in the instant application. Therefore, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

D. Fleming in view of U.S. Patent Application Publication No. 2003/0185796 A1, further in view of Sosman

Claims 18, 19, 38-40, 42-47, 61, 62, 69, and 70 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Fleming et al. (Abstract No. 710, Program Proceedings, American Society of Clinical Oncology, 35th Annual Meeting, 1999) as evidenced by Fleming et al. (Clin. Cancer Res. (2002) 8:3718-3727) in view of U.S. Patent Publication No. 2003/0185796, and further in view of Sosman et al. (J. Clin. Oncol. (1993) 11:1496-1505). Applicants respectfully traverse the rejection.

Applicants reiterate that the Declaration of the inventors Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky under CFR § 1.132 is entitled to consideration. The inventors of the present application, Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, are

coauthors on the Fleming et al. ASCO abstract. The relevant portions of Fleming et al. describe applicants' own work, and the remaining co-authors on the abstract are not inventors of the subject claims (see Declaration of Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, pursuant to *In re Katz*, previously submitted on September 1, 2006).

As mentioned above, the secondary reference of U.S. Patent Publication No. 2003/0185796 fails to describe or suggest any method of treating cancer using concurrent therapy with a combination of an anti-HER2 antibody and IL-2. Sosman also fails to describe or suggest the claimed methods. Sosman pertains to methods of treating metastatic melanoma with anti-CD3 antibodies. No mention is made of anti-HER2 antibodies. Combinations of these references would lead the practitioner to a dosing regime using IL-2 and an anti-CD20 antibody for treating metastatic cancer or alternatively, IL-2 and an anti-CD3 antibody for treating non-Hodgkin's lymphoma, not to a combination of IL-2 or a variant thereof and an anti-HER2 antibody comprising the CDR regions of a 4D5 or 520C9 antibody for treating breast cancer, as taught in the instant application. There is no showing of *prima facie* obviousness. Therefore, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

E. Fleming in view of U.S. Patent Application Publication No. 2003/0185796 A1, Sosman, and Soiffer

Claims 20, 21, 41, 48-50, 71, and 72 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Fleming et al. (Abstract No. 710, Program Proceedings, American Society of Clinical Oncology, 35th Annual Meeting, 1999) as evidenced by Fleming et al. (Clin. Cancer Res. (2002) 8:3718-3727) in view of U.S. Patent Publication No. 2003/0185796 and Sosman et al. (J. Clin. Oncol. (1993) 11:1496-1505, and further in view of Soiffer et al. Clin. Cancer Res. (1996) 2:493-499). Applicants respectfully traverse the rejection.

Applicants reiterate that the Declaration of the inventors Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky under CFR § 1.132 is entitled to consideration. The inventors of the present application, Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, are coauthors on the Fleming et al. ASCO abstract. The relevant portions of Fleming et al. describe applicants' own work, and the remaining co-authors on the abstract are not inventors of the

subject claims (see Declaration of Michael Caligiuri, Neal J. Meropol, and Richard L. Schilsky, pursuant to *In re Katz*, previously submitted on September 1, 2006).

As discussed above, neither U.S. Patent Publication No. 2003/0185796 nor Sosman describe or suggest the claimed methods of treatment. Soiffer also fails to describe or suggest any method of treating cancer using concurrent therapy with a combination of an anti-HER2 antibody and IL-2. Rather, Soiffer teaches the use of IL-2 in patients with metastatic cancer, where the patients being treated have renal cell carcinoma, melanoma, lung cancer, colon cancer, sarcoma, nonseminomatous germ cell tumor, or chronic mylegenous leukemia. Nowhere does Soiffer suggest a combination of IL-2 or a variant thereof and an anti-HER2 antibody, and there is no motivation, nor any expectation of success suggested in the combination of these references. Furthermore, there is no showing of *prima facie* obviousness. Therefore, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

35 U.S.C. § 112, second paragraph

Claims 74-79 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." (Final Office Action, page 39). In particular, the Final Office Action alleges that claims 74-79 are indefinite because of the recitation of the trademark Herceptin®:

> The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. In the present case, the trademark/trade name is used to identify/describe the recombinant, humanized anti-HER2 antibody derived from the murine monoclonal antibody 4D5 and, accordingly, the identification/description is indefinite. (Final Office Action, page 39.)

Applicants respectfully traverse the rejection.

According to M.P.E.P. § 608.01(v), trademarks are permissible in applications under certain conditions:

> Names used in trade are permissible in patent applications if:

> (A) Their meanings are established by an accompanying definition which is sufficiently precise and definite to be made a part of a claim, or
>
> (B) In this country, their meanings are well-known and satisfactorily defined in the literature.
>
> Condition (A) or (B) must be met at the time of filing of the complete application.

Applicants submit that the current claims comply with these criteria. Claims 74-79 have been amended to make explicit that the anti-HER2 antibody is Herceptin® recombinant humanized 4D5 monoclonal antibody. Hence, the Herceptin® trademark is accompanied by a definition and is appropriate in the claim to sufficiently identify the particular anti-HER2 antibody formulation intended. Moreover, the Herceptin® formulation was known in the art at the time of filing of the instant application and is described in the specification, for example, at page 29, lines 21-24.

For at least these reasons, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

35 U.S.C. § 112, first paragraph, New Matter

Claims 12-50, 52, 53, 55, 56, 58, 59, and 61-79 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (Final Office Action, page 39).

A. Polypeptide Comprising SEQ ID NO:1

The Final Office Action alleges that the original disclosure does not provide support for the recitation of the amino acid sequence of SEQ ID NO:1 in claims 12, 16, 17, 42, and 63:

> Thus, while the inclusion of SEQ ID NO:1 in the claims finds support in the specification, as amended September 1, 2006, the original disclosure provides no apparent nexus between the amino acid sequence set forth as SEQ ID NO:1 and the amino acid sequence of the native human IL-2 molecule, which might serve as a basis for the amendment to the specification. If, as explained above, the amendment to the specification finds no written support in the specification, including the claims, as

> originally filed, then amending the claims to recite "SEQ ID NO:1" introduces new matter and thereby violates the written description requirement set forth under 35 U.S.C. § 112, first paragraph. (Final Office Action, page 28.)

Applicants respectfully traverse the rejection.

As discussed above regarding the objection under 35 U.S.C. § 132, the specification need not recite a sequence, nor incorporate it by reference, if the sequence is known in the prior art. See, *e.g.*, *Falkner v. Inglis*, 79 USPQ2d 1001, page 1009 (Fed. Cir. 2006). The sequence of human IL-2 was well-known at the time of filing of the instant application (see, *e.g.*, Figure 2b of U.S. Patent No. 4,738,927, which was cited in the instant application, for example, at page 17, line 13, and incorporated by reference; and GenBank Accession No. S82692). The definition of IL-2 presented at page 12, lines 8-19 of the specification is clearly intended to encompass the human native mature active form of IL-2. The specification refers to biologically active variants of IL-2 with reference to a native IL-2 polypeptide (see, *e.g.*, page 13, lines 21-22; and page 14, lines 11-26). Applicants further note that at page 29, lines 1-11 of the specification, the IL-2 mutein aldesleukin is described with reference to the sequence of the native mature active form of IL-2. Therefore, the claimed subject matter has adequate descriptive support in the original disclosure of the specification. Withdrawal of the new matter rejection under 35 U.S.C. § 112, first paragraph on this basis is therefore respectfully requested.

B. Biologically Active Variants of IL-2

The Final Office Action alleges that the specification does not provide written support for the recitation of variants of IL-2 comprising an amino acid sequence having at least 90% sequence identity to SEQ ID NO:1 in claims 12, 16, 17, and 42:

> However the particular disclosure at page 14 of the specification does not provide written support for variants of a polypeptide comprising the amino acid sequence of SEQ ID NO:1, per se, nor does it provide written support for variants of such a polypeptide comprising amino acid sequences that are at least 90% identical to amino acid sequence of that polypeptide (i.e., SEQ ID NO:1). Moreover, it appears that the specification only provides written support for suitable biologically active variants of native and naturally occurring IL-2, including "fragments", analogues", and "muteins", as opposed to variant of an IL-2 molecule comprising the amino acid sequence of SEQ ID NO:1; see, in particular, page 13, lines 6 and 7. (Final Office Action, page 41).

Applicants respectfully traverse the rejection.

Claims 12, 16, 17, and 42 have been amended to make explicit that the recited variants of IL-2 have at least 90% sequence identity to SEQ ID NO:1. As discussed above, SEQ ID NO:1 in the revised Sequence Listing now corresponds to the sequence of native mature human IL-2. The specification provides support for variants having at least 90% identity to a native IL-2 polypeptide, such as a polypeptide having the sequence of SEQ ID NO:1 (see specification, for example, at page 14, lines 11-26). The definition of IL-2 presented at page 12, lines 8-19 of the specification is clearly intended to encompass the human native mature active form of IL-2. Applicants submit that the claimed subject matter is fully supported by the application as originally filed.

C. Recitation of Antibodies that Bind the Same Epitope as 4D5 or 520C9

The Final Office Action alleges that the specification does not provide written support for the recitation of antibodies that bind the same epitope as 4D5 or 520C9 in claims 12, 16, 17, and 42:

> The specification fails to disclose the subgenus of antibodies that binds to the epitopes of HER2 to which the monoclonal antibodies 4D5 and 520C9 bind, which excludes other antibodies that bind different epitopes of HER2 not recognized by either one of these particular antibodies. (Final Office Action, page 43.)

In order to expedite prosecution, Applicants have amended claims 12, 16, 17, and 42 to make explicit that the anti-HER2 antibody comprises a complementarity determining region (CDR) of an anti-HER2 antibody selected from the group consisting of 4D5 (ATCC Number CRL-10463) and 520C9 (ATCC Number HB-8696), wherein said anti-HER2 antibody binds to the extracellular domain of the HER2 receptor protein. Support for this amendment can be found in the specification, for example, at page 21, lines 23-25; page 22, line 11 through page 23, line 25; and page 29, lines 15-17. Withdrawal of the new matter rejection under 35 U.S.C. § 112, first paragraph on this basis is therefore respectfully requested.

CONCLUSION

In light of the above remarks, Applicants submit that the present application is fully in condition for allowance. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned.

The Commissioner is hereby authorized to charge any fees and credit any overpayment of fees which may be required under 37 C.F.R. §1.16, §1.17, or §1.21, to Deposit Account No. 18-1648.

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Cell Biology

Structural homologies among the hemopoietins

(colony-stimulating factors/interleukins/P-cell-stimulating factor/amino acid sequence)

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ABSTRACT **A group of cytokines characterized by a common set of target cells—namely, the pluripotential hemopoietic stem cells or their cellular derivatives—share similarities in the amino acid sequence at their N terminus or in the putative signal peptide immediately prior to the published N terminus. Murine P-cell-stimulating factor (PSF), murine and human interleukin 2 (IL-2), murine and human granulocyte–macrophage colony-stimulating factor (GM-CSF), human erythropoietin, and human interleukin 1β all share alanine as the N-terminal amino acid and have some similarities in the succeeding three or four amino acids. In the case of murine PSF and GM-CSF, the six N-terminal amino acids are readily cleaved from mature molecules and are lacking from the N-terminal amino acid sequences reported initially. A sixth cytokine, colony-stimulating factor 1, has an alanine followed by a similar pattern of five amino acids at the end of the putative signal peptide. GM-CSF and IL-2 have more extensive homology, about 25% of residues being identical in three regions that comprise about 70% of the molecules. Only minor similarities of uncertain significance were found among the complete amino acid sequences of the other cytokines. Although its evolutionary origin is uncertain, the homology around the N terminus may provide a structural marker for a group of cytokines active on the pluripotential hemopoietic stem cell and its derivatives.**

The pluripotential hemopoietic stem cell gives rise to the erythrocytes, granulocytes, monocytes, and lymphocytes of the blood and to a variety of tissue cells, including macrophages, mast cells, and probably dendritic cells and Langerhans cells (1). The growth and differentiation of pluripotential hemopoietic stem cells and their cellular derivatives are influenced by a series of soluble polypeptides or cytokines (1, 2), a number of which have now been purified and molecularly cloned. These include interleukin 2 (IL-2) (3–6), P-cell-stimulating factor (PSF) or interleukin 3 (IL-3) (7–10), granulocyte–macrophage colony-stimulating factor (GM-CSF) (11–13), colony-stimulating factor 1 (CSF-1) (14), erythropoietin (EPO) (15), and interleukin 1 (IL-1), in which case two related forms, IL-1α and IL-1β, have been cloned (16–18).

These cytokines, together with several well-characterized related factors for which amino acid sequence data are not at present available, such as granulocyte-CSF (19), B-cell growth factor (20), and eosinophil-differentiating factor (21), share a number of broad biological and structural similarities. Most are glycoproteins with an apparent M_r of 15,000–35,000 on gel filtration, although CSF-1 occurs as a large dimer (14). In most cases the biologically active polypeptide chain consists of about 140 amino acid residues. However, despite these superficial similarities in molecular structure, analyses of amino acid sequences have not yet revealed any homology, either within this group of cytokines or with any other known protein sequences.

Here we report that, contrary to these previous conclusions, there is evidence of structural homology at or adjacent to the N terminus of a group of cytokines active on cells of hemopoietic origin. Moreover, in the case of IL-2 and GM-CSF, there is also significant homology over much of the remainder of the molecule. The homology in regions at or adjacent to the N termini of these cytokines may reflect their interaction with a common structure or related group of structures and may define a functional group of cytokines.

RESULTS

A Cleavable Hexapeptide at the N Termini of PSF and GM-CSF. One key to the present observations was the discrepancy between the reported N-terminal amino acid sequences of PSF (7) and IL-3 (8), both of which are encoded by the same gene (9, 10). Comparison of the sequences of PSF (7) and IL-3 (8) indicates that PSF has an additional six amino acids at the N terminus. As shown in Fig. 1, the N-terminal amino acid residue of PSF was determined to be alanine (solid arrow), whereas that of IL-3 was the aspartic acid at position 7 of PSF (dotted arrow). We have postulated (7) that the IL-3 form of the molecule results from proteolytic cleavage of PSF at the bond between arginine and aspartic acid at positions 6 and 7.

A similar discrepancy in data on the N-terminal amino acid sequence of GM-CSF indicated that the cleavage of a small peptide from the N terminus was not unique to PSF. As shown in Fig. 1, the N-terminal amino acid sequence of murine asialo-GM-CSF (11, 22) (dotted arrow) differed from that subsequently reported for human GM-CSF (12, 13) (solid arrow) (Fig. 1). Based upon the N-terminal amino acid sequence of human GM-CSF it was suggested that murine GM-CSF might in fact include an additional six amino acids (12, 13). Subsequent analysis of murine GM-CSF indicated that this was indeed the case and that, as in the human, the N-terminal residue of murine GM-CSF was an alanine (23). This alanine occurred six residues N-terminal to the isoleucine that was initially reported as the N terminus (11, 23) and it was concluded that the original result reflected cleavage of the N-terminal six amino acid residues during production or purification of the GM-CSF (23).

CSF-1. Based upon the amino acid sequence deduced from the cDNA clone, Kawasaki *et al.* (14) concluded that CSF-1 was unrelated to other cytokines or proteins. However, as shown in Fig. 1, at the end of the putative signal peptide there is a short region with some similarities to the N terminus of PSF. Thus, six residues from the glutamic acid, which Kawasaki *et al.* identified as the N terminus, there is an alanine and, of the next three residues, two are serines that can be aligned with the serines at positions 2 and 4 in PSF

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Abbreviations: CSF, colony-stimulating factor; EPO, erythropoietin; GM-CSF, granulocyte–macrophage colony-stimulating factor; IL, interleukin; PSF, P-cell-stimulating factor.

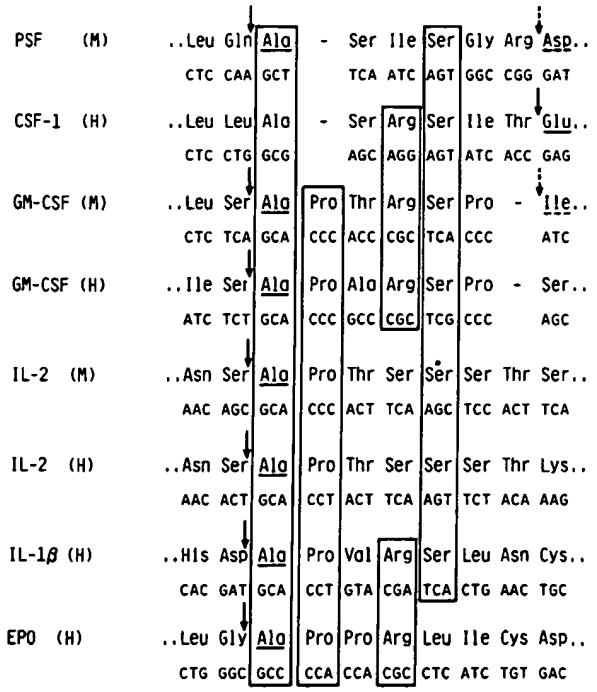

FIG. 1. Sequences at or adjacent to the N termini of six cytokines of human (H) or murine (M) origin. N-terminal residues are underlined and the cleavage sites of the signal peptides are indicated by solid arrows. Broken underlining and arrows indicate the alternative N termini that have been reported for IL-3 (8) or murine asialo-GM-CSF (11, 22).

(Fig. 1). This observation raises the possibility that, as in the case of PSF and murine GM-CSF, a hexapeptide had been cleaved from the material that had been sequenced and that the N terminus of mature CSF-1 may be alanine.

The N Termini of IL-2 and EPO. In the cases of murine and human IL-2 the N-terminal amino acid was once again alanine (3–6). Moreover, there was a striking pattern of homology with the N termini of murine and human GM-CSF. Of the four amino acids following the alanine, three were identical in murine and human IL-2 and murine GM-CSF, forming the pattern Ala-Pro-Thr-Xaa-Ser. Human GM-CSF differed slightly in that a single base change had resulted in the substitution of an alanine for the threonine (Fig. 1).

Inspection of the N-terminal amino acid sequence of human EPO once again revealed that the N-terminal amino acid was alanine and that the second residue was proline, as in the case of IL-2 and GM-CSF. The fourth residue, arginine, was identical with the fourth residue of GM-CSF and IL-1β (see below) (Fig. 1).

Homology at or Adjacent to the N Termini of Other Proteins and Cytokines. Based upon these observations, which suggested that a group of cytokines was characterized by the presence of a common pattern of amino acids around the N-terminal amino acid sequence, we used the SEARCH computer program (24) to locate other proteins containing peptides of patterns APTXS, APSXS, ATXS, ASXS, and APXR, where the letters represent the single-letter amino acid code and X represents an unspecified residue. Homology was scored using the mutational data matrix for 250 accepted point mutations (25). The 100 top-scoring sequences were selected for further visual examination.

In only 1 of the 3477 sequences available in the NIH protein-sequence database of The Protein Identification Resource was one of the searched patterns located at the N terminus of a molecule. Remarkably, the sequence involved was that of a cytokine, IL-1β, which had the N-terminal amino acid sequence Ala-Pro-Val-Arg-Ser (Fig. 1).

We also examined the sequences of a number of other cytokines. Interferon γ showed no evidence of homology at the N terminus or in the signal peptide region. Likewise, a homologous peptide was absent in lymphotoxin, tumor-necrosis factor, and also insulin, insulin-like growth factors, and relaxin. The pentapeptide Ala-Pro-Ser-Arg-Ala, however, occurs at the end of the putative signal peptide of the human tissue inhibitor of metalloproteinases (26), which has also been termed erythroid-potentiating activity (EPA) (27) because it promotes the formation of colonies of erythroid cells in bone marrow cultures. Although EPA has been classified as a hemopoietin (27), this point requires clarification as a direct action on erythroid progenitors has not been demonstrated and it is conceivable that its effects on erythropoietic cells *in vitro* are indirect and related to its action as a proteinase inhibitor. Moreover, according to the empirical rules of van Heijne (28), it is unlikely that cleavage of a signal peptide would occur between the first alanine of this pentapeptide and the isoleucine of the preceding sequence—Trp-Leu-Ile-. Thus, on balance, EPA is not likely to be a member of this group of cytokines.

Homology in Other Regions of GM-CSF and IL-2. When the sequences of IL-2 and GM-CSF of murine and human origin were aligned at the N and C termini and gaps introduced, there were multiple identities (Fig. 2).

There were matches between at least one of the two GM-CSF sequences and one of the two IL-2 sequences at about 28% of residues. If human GM-CSF was compared with murine IL-2 or human IL-2 there were identities in 17% and 18% of positions, respectively. Figures were similar if mouse GM-CSF was compared with human IL-2 or mouse IL-2 (20%) and (17%), respectively.

If the regions where the sequences appear to differ radically (i.e., those corresponding to residues 35–48 and 73–95 of human GM-CSF) were excluded, in the remaining 70% of the molecules there were identities between at least one of the GM-CSF sequences and one of the IL-2 sequences at 40% of positions. Table 1 shows in more detail the degree of homology between GM-CSF and IL-2 in these three regions. The similarities between the sequences of GM-CSF and IL-2 were even greater if instances were taken into account where amino acid differences could be accounted for by single base changes at the codon level or involve functionally related amino acids.

DISCUSSION

These observations on a group of cytokines that has as its targets the pluripotential hemopoietic stem cell or its cellular derivatives fall into two main categories. (*i*) There is the demonstration that there is a group of cytokines that share a short homologous peptide at the N terminus that has the pattern Ala-Ser-Xaa-Ser or Ala-Pro-Xaa-Arg(or Ser)-Ser(or Leu). In the case of GM-CSF and PSF the six N-terminal amino acids are readily cleavable, raising the possibility that a homologous hexapeptide at the end of the putative signal peptide of CSF-1 also represents an N-terminal hexapeptide that is readily cleavable from the native molecule. (*ii*) There is the demonstration that two cytokines in this group, IL-2 and GM-CSF, show significant homology over the greater part of the molecules. Both sets of observations demand reassessment of the prevailing view that these cytokines lack homology and raise the possibility of functional interrelationships between the members of this group.

A number of arguments makes it extremely unlikely that the pattern of homology around the N termini of these molecules has occurred by chance alone. Merely the obser-

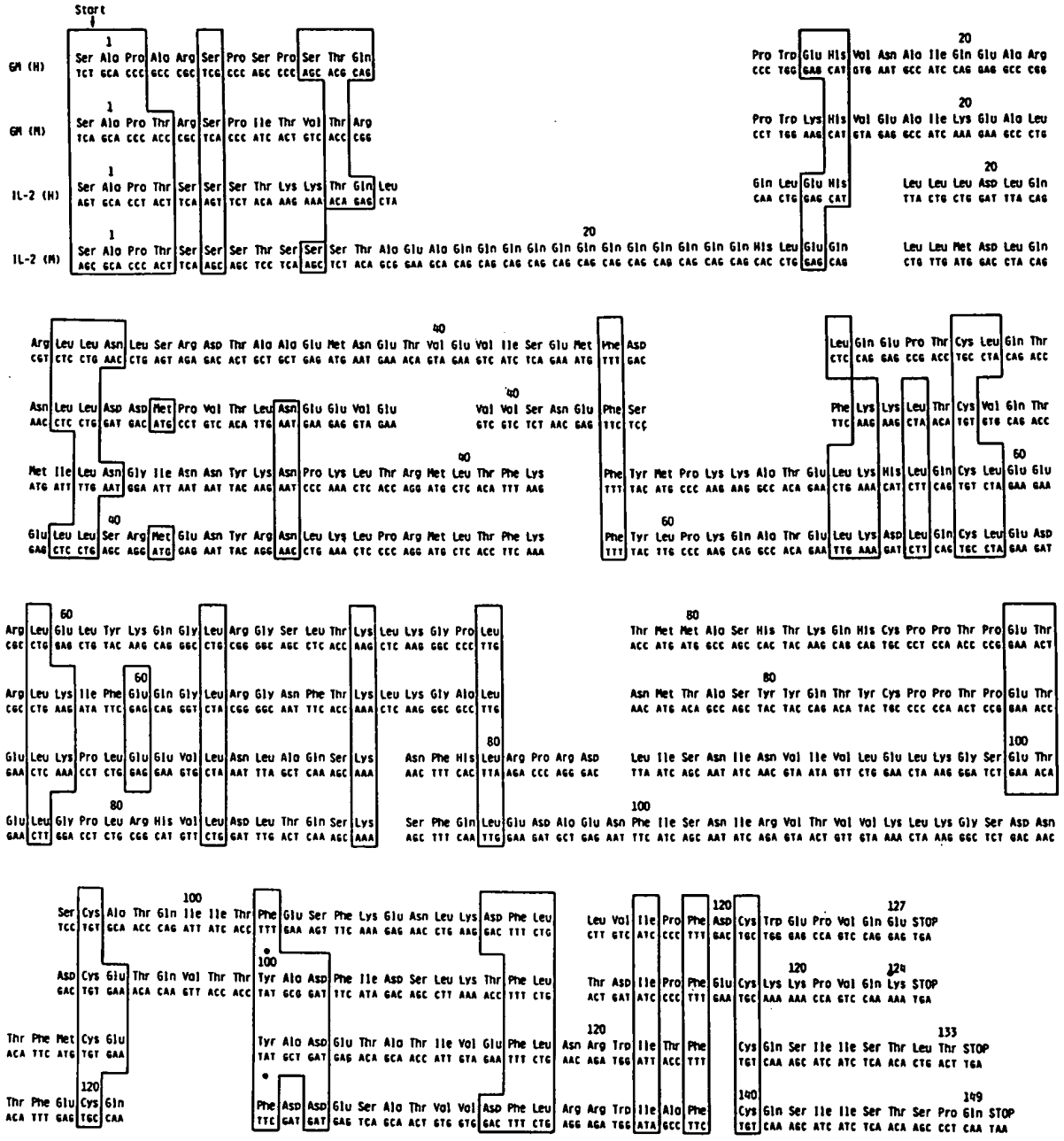

FIG. 2. Amino acid sequence homology of human (H) and murine (M) GM-CSF and IL-2. In aligning the four sequences, gaps were introduced to maximize homology. Sequences are numbered from the N-terminal alanine of the mature proteins.

vation that the five cytokines PSF, GM-CSF, IL-2, EPO, and IL-1β share alanine as their N-terminal amino acid residue suggests that this part of the molecule may be under some common selective pressure. Based upon the NIH protein-sequence database the frequency of alanine in proteins of higher primates is 0.065. Accordingly, probability that four randomly selected human molecules would resemble PSF in sharing alanine as the N-terminal amino acid, as do GM-CSF, IL-2, EPO, and IL-1β, is only 1.8×10^{-4}. The fact that the N-terminal alanine is conserved across species in the human and mouse in the case of GM-CSF and IL-2 (Fig. 1) adds further weight to the notion that the alanine at this position has a particular functional significance. There is no evidence that alanine is in general overrepresented at the N terminus of secreted proteins, and alanine occurred at a frequency of about 0.08 in the collection of secreted proteins studied by van Heijne (28).

Similarities in the pattern of amino acids following the alanine in Fig. 1 further strengthen the notion that the N termini of PSF, GM-CSF, IL-2, and IL-1β are homologous. Some indication of the very low probability that this situation could occur by chance alone can be gained by considering the likelihood of identities at particular positions in two randomly chosen peptides of six amino acids. Based on the relative frequencies of the various amino acids in rodents and higher primates, the probability of any match at a particular position

Table 1. Homologous regions of GM-CSF and IL-2

	% identical amino acids in homologous regions				
Region*	GM-CSF (M or H) and IL-2 (M or H)	GM-CSF (H) and IL-2 (M)	GM-CSF (H) and IL-2 (H)	GM-CSF (M) and IL-2 (M)	GM-CSF (M) and IL-2 (H)
1–34	44	24	29	26	26
49–72	42	25	25	25	33
96–127	34	25	22	22	31
All†	40	24	26	24	30

H, human; M, murine.
*Regions corresponding to the indicated residues of human GM-CSF as aligned in Fig. 1.
†Sum of regions indicated above.

is 0.0579 for mice and 0.0581 for humans. By using the relevant binomial distributions, the probability that two such random hexapeptides would be identical at greater than or equal to three positions is 1.5×10^{-4} (for higher primate sequences) and 1.6×10^{-4} (for rodent sequences). The probability of four or greater than four identities is 4×10^{-6} for higher primates and rodents. Of the six N-terminal amino acids of GM-CSF and IL-2, four are identical in the mouse ($P = 4 \times 10^{-6}$) and three in the human ($P = 1.5 \times 10^{-4}$). The six N-terminal residues of GM-CSF and IL-1β in the human are identical at four positions ($P = 4 \times 10^{-6}$) and the six N-terminal residues of human IL-2 and IL-1β are identical at three positions ($P = 1.5 \times 10^{-4}$). If, as in Fig. 1, we align the reported N termini and the preceding six amino acids of the putative signal peptides of CSF-1 (14) and IL-3 (8), there are identities at three positions. It should be noted that none of the identities considered above depends upon the insertion of the gap in the sequences.

The fact that a computer search of a database of 3477 proteins located a related sequence at or adjacent to the N terminus of only one other protein further supports the notion that the occurrence of these patterns around the N terminus of PSF, GM-CSF, IL-2, CSF-1, and EPO is not coincidental. This conclusion is enhanced by the fact that the sequence located was that of another cytokine, IL-1β.

The relationship of IL-1β to the other molecules shown in Fig. 1 is worthy of comment. Unlike other cytokines and indeed all other secreted proteins, IL-1β lacks a signal peptide with the characteristic stretch of hydrophobic amino acids (16). IL-1β may also differ from the other cytokines in Fig. 1 in having other targets in addition to derivatives of the pluripotential hemopoietic stem cell (16). The published data on the biological activity of IL-1β derived from cloned cDNA relate to its action on T lymphocytes, but further experiments should establish whether IL-1β acts directly on cells of nonhemopoietic origin such as hepatocytes or fibroblasts. Information on this question and data on the amino acid sequences at the N terminus of IL-1β in other species may help in deciding whether the striking similarity of IL-1β with the other cytokines in Fig. 1 is coincidental.

The fact that in the cases of PSF and GM-CSF the homologous peptide is present on the secreted molecule, but appears to be readily cleaved off, raises the question of whether a similar phenomenon occurs with the other factors in Fig. 1. It will be interesting to determine whether the published N-terminal amino acid sequence of CSF-1 also represents the sequence of a cleaved form of the secreted protein. The published N terminus is consistent with the empirical rules governing the cleavage sites of signal peptides proposed by van Heijne (28). However the cleavage sites established for other cytokines in Fig. 1 make it reasonable to postulate a cleavage site between the leucine and the alanine aligned with the N-terminal alanines of the other cytokines in Fig. 1. A related question is whether there are shorter forms of IL-2 molecules that lack an N-terminal peptide, the published sequences of IL-2 corresponding to a long, more abundant form.

The function of the homologous regions at the N termini of these cytokines is unknown but presumably reflects interaction of these molecules with a common structure or closely related set of structures. One possibility is that cleavage of the homologous peptide from these cytokines allows the further metabolic processing or excretion of the molecule. It is interesting in this respect that the N-terminal amino acid sequence of CSF-1 was determined on material obtained from urine (14). Certainly it is unlikely that the homologous peptide is involved in the primary biological activity of the various molecules because the short forms of PSF (IL-3) (8) and GM-CSF (11, 22) lacking the homologous peptide are fully biologically active, at least *in vitro*.

The question of whether the similarities at the N termini reflect convergent evolution or divergent evolution cannot be resolved on the data available. The more extensive homology between GM-CSF and IL-2, however, favors a common evolutionary origin of at least these two members of the group. We have observed some other homologies between CSF-1, PSF, GM-CSF, and IL-2, but more refined analyses and additional data on sequences from other species will be necessary to establish whether they have any significance.

Analysis of the three cysteines that may be conserved in human IL-2 and GM-CSF (the latter having an additional cysteine at position 88) may assist in the elucidation of the secondary structure of GM-CSF. Thus, in IL-2 the cysteines at positions 58 and 105 are paired (29) and the cysteine at position 125 can be substituted with a serine without impairing biological activity (30). By analogy, it might be predicted that in GM-CSF the corresponding cysteines at positions 54 and 96 are paired and are critical for maintaining the biologically active structure.

The fact that a group of cytokines that share a common set of targets, the pluripotential hemopoietic stem cell or its derivatives, also share similarities at the N termini provides a new parameter for classifying cytokines. The evidence of structural homology between GM-CSF, which acts on myeloid cells, and IL-2, generally regarded as acting between lymphocytes, highlights the unsatisfactory nature of the present nomenclature, which has tended to distinguish between factors studied by hematologists and those by immunologists. One option is that the general term "hemopoietin" be adopted for this entire group of molecules. Individual members could then be identified by numbers (hemopoietin 1, etc.).

It could be argued that hemopoietin is an unsuitable term for molecules that affect lymphocytes. Lymphocytes, however, are a major cellular product of the bone marrow (1) and, like other blood cells, are derived from the pluripotential hemopoietic stem cell. There are many structural similarities between lymphocytes and other derivatives of the pluripotential hemopoietic stem cell, such as Thy-1 and Ly-5 antigens (1). The close developmental relationship between these derivatives of the pluripotential hemopoietic stem cell is also emphasized by evidence that limited rearrangement of DNA in the region of the genes for the T-cell receptor can occur in myeloid cells (31) and that transcription of the μ heavy chain gene can occur in macrophages (32). Moreover, IL-2 receptors have been detected on certain lines of macrophage (33) and mast cell origin (34), suggesting that IL-2 may not act exclusively on the lymphoid component of the hemopoietic system. A simple unified system of nomenclature would have much to recommend it; the present data suggest that structural similarities may be helpful in defining a group of molecules.

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Medical Sciences

Human T-cell growth factor: Partial amino acid sequence, cDNA cloning, and organization and expression in normal and leukemic cells

(DNA sequence/plasmid expression)

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ABSTRACT **The partial amino acid sequences of human T-cell growth factors (TCGFs) isolated from normal peripheral blood lymphocytes and from a leukemia T-cell line (Jurkat) show that the amino-terminal sequences of the two proteins (15 residues) are identical. Oligonucleotides based on the published Jurkat TCGF DNA sequence were used to isolate six cDNA clones of TCGF mRNA from normal lymphocytes. The predicted amino acid sequence of normal lymphocyte TCGF was identical to the sequence of the Jurkat protein, showing that the differences in biochemical properties of the two proteins result from post-translational events. Amino acid and nucleotide sequence data suggest that TCGF is derived from a precursor polypeptide that is cleaved at the amino terminus but not at the carboxyl terminus. Hybridization of the cloned lymphocyte TCGF cDNA to cellular DNA and RNA strongly suggested that the TCGF gene is expressed as a single mRNA species from a single-copy gene. No differences in the organization of the TCGF gene in normal, leukemic, and human T-cell leukemia/lymphoma virus-infected cells was detected regardless of whether they produce TCGF or not.**

T-cell growth factor (TCGF), also called interleukin 2, is a protein that supports the proliferation of activated T cells (1, 2). Its use has allowed the development of systems for long-term growth of T-cell populations of defined function and specificity (2, 3), thus facilitating studies of cellular immunity and possible clinical immunotherapeutic applications (4). The ability to grow some forms of neoplastic mature T cells with TCGF directly led to the isolation of a retrovirus termed human T-cell leukemia/lymphoma virus (5–7). Human TCGF is a polypeptide of ≈15,000 daltons produced by normal peripheral blood lymphocytes (PBL) (8) and certain leukemic T-cell lines (e.g., Jurkat) (9) after appropriate stimulation, while some retrovirus-infected mature neoplastic T-cell lines (10) and a gibbon T-cell lymphoma line (11) produce TCGF constitutively. Minor heterogeneities have been detected in human TCGF produced from different cells (10). The normal lymphocyte and leukemic Jurkat TCGFs differ in such biochemical properties as isoelectric focusing (pI values of 6.8 and 8.2 for PBL and Jurkat TCGF, respectively) (2, 3) and hydrophobicity as judged by reversed-phase HPLC (12). These could result from post-translational modification of the protein or polymorphism of the gene itself. It is possible that TCGF, like the interferons (13), is a mixture of similar products derived from a moderately large gene family, only one of which is expressed in a given cell type. Further understanding of the structure of TCGF and of the molecular mechanism of immune regulation as well as large-scale production of the protein for clinical use would be facilitated by molecular cloning of the gene. Taniguchi *et al.* (14) recently succeeded in obtaining a full-length cDNA clone of a Jurkat mRNA that encodes active TCGF. To clone TCGF mRNAs from normal human PBL, synthetic oligonucleotides based on the published Jurkat TCGF DNA sequence (14) were used to probe a cDNA library. Six overlapping clones thus obtained were characterized and their nucleotide sequence was compared with the published sequence of the Jurkat cDNA clone. The cloned TCGF sequence was also used to analyze the structure of this gene in the human genome, to determine whether modifications of the gene could be found in certain diseases, and to find the pattern of its expression in different human cell types.

MATERIAL AND METHODS

Purification and Amino Acid Sequence Analysis. NH_2-terminal amino acid sequence was determined by Edman degradation using a micro procedure (15). Additional sequence data for Jurkat TCGF were obtained by endopeptidase Lys C digestion of *S*-carboxamidomethylated protein followed by sequencing of the specific peptides (15).

cDNA Cloning, Expression, and DNA Sequence Analyses. cDNA of poly(A)$^+$ RNA from phytohemagglutinin and phorbol myristate acetate stimulated normal human PBL was cloned in pBR322 by standard procedures (16). A library of 40,000 clones was replica plated, amplified with chloramphenicol (17), and screened by a colony hybridization procedure (18) using labeled oligonucleotides as probes. The hybridization reaction mixture contained 4× NaCl/Cit (1× NaCl/Cit = 0.15 M NaCl/0.015 M Na citrate, pH 7), 5× PM (PM = 0.02% Ficoll 400/polyvinylpyrrolidone/bovine serum albumin), herring sperm DNA at 100 μg/ml, 0.1% NaDodSO$_4$, and ^{32}P-labeled oligonucleotide at 10^5 cpm/ml (10^8 cpm/pmol); reaction mixtures were incubated overnight at 30°C.

The TCGF cDNA insert was introduced into the expression vector pCVSVL (19) at the *Pst* I site and amplified in *Escherichia coli* strain HB101. The hybrid DNA (8 μg) was applied to a subconfluent monolayer of monkey COS-7 cells in a 10-cm dish by the DEAE-dextran transfection protocol (19, 20). The transfected cells were incubated for 48 hr and conditioned medium and cell extracts were assayed for

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Abbreviations: TCGF, T-cell growth factor; PBL, peripheral blood lymphocyte(s); bp, base pair(s); kb, kilobase(s); NaCl/Cit, 0.15 M NaCl/0.015 M Na citrate, pH 7.

‡To whom reprint requests should be addressed.

Table 1. Partial amino acid sequences of Jurkat and PBL TCGFs

Intact protein	
PBL (1–15)	Ala-Pro- X -Ser-Ser-Ser-Thr-Lys-Lys-Thr-Gln-Leu-Gln-Leu-Glu
Jurkat (1–25)	Ala-Pro- X -Ser-Ser-Ser-Thr-Lys-Lys-Thr-Gln-Leu-Gln-Leu-Glu-His-Leu-Leu-Leu-Asp-Leu-Gln-Met-Ile-Leu
Jurkat COOH terminus (132 and 133)	Leu-Thr
Jurkat peptide	
A (1–8)	Ala-Pro- X -Ser-Ser-Ser-Thr-Lys
B (49–54)	Lys-Ala-Thr-Glu-Leu-Lys
C (44–47)	Phe-Tyr-Met-Pro
D (36–43)	Leu-Thr-Arg-Met-Leu-Thr-Phe-Lys
E (55–74)	His-Leu-Gln-Cys-Leu-Glu-Glu-Glu-Leu-Lys-Pro-Leu-Glu-Glu-Val-Leu-Asn-Leu-Ala-Gln
F (10–17)	Thr-Gln-Leu-Gln-Leu-Glu-His-Leu
G (77–93)	Asn-Phe-His-Leu-Arg-Pro-Arg-Asp-Leu-Ile-Ser-Asn-Ile-Asn-Val-Ile-Val

Numbers in parentheses indicate positions in the complete sequence (Fig. 1).

TCGF activity by measuring [^{3}H]thymidine incorporation by TCGF-dependent murine CTLL cells (21).

The DNA sequence was determined by a combination of M13 dideoxy (22) and standard degradation (23) methods.

Southern and RNA Blot Hybridization. High molecular weight DNA was isolated as described (24). RNA was isolated by guanidine·HCl extraction (25) followed by CsCl centrifugation (26) and oligo(dT)-cellulose chromatography as described (27). For Southern blotting (28), DNA was digested with a restriction enzyme, electrophoresed, transferred to a cellulose nitrate sheet (28), and hybridized overnight at 37°C with nick-translated cloned TCGF DNA in a mixture

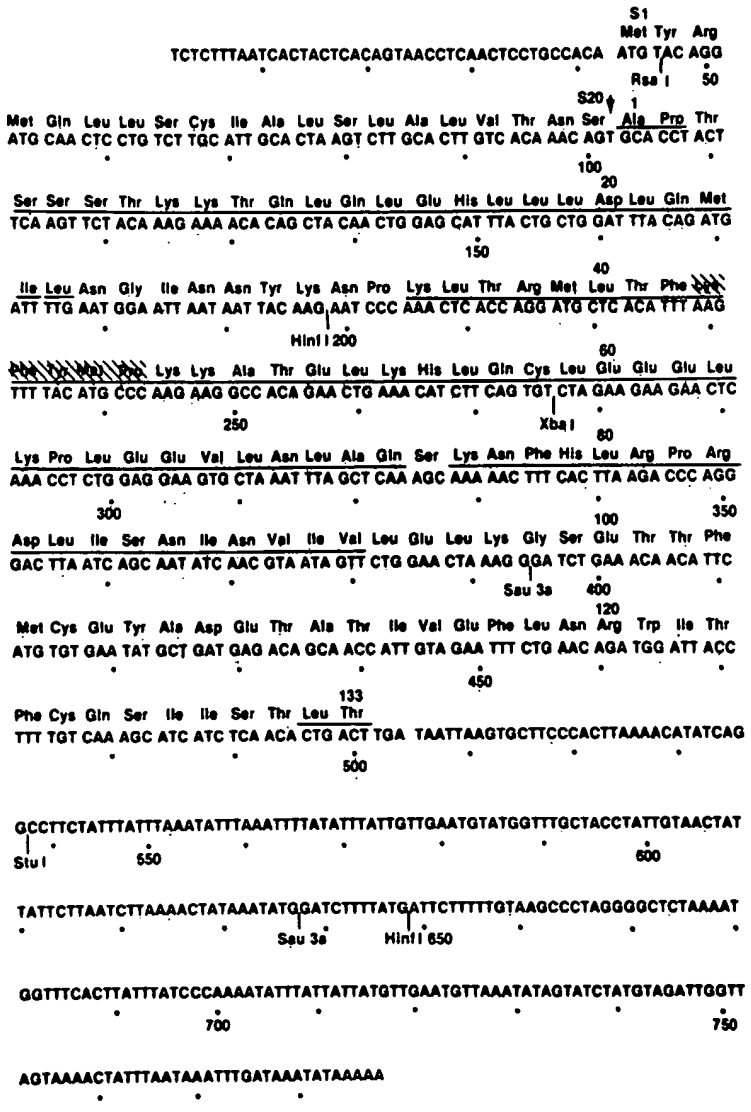

FIG. 1. Sequence of human PBL TCGF cDNA clones pTCGF-11 and pTCGF-5. The sequence of pTCGF-5 is shown and that of pTCGF-11 begins with nucleotide 25 and continues to the end of the sequence shown. Above the DNA sequence we have shown the deduced amino acid sequence of PBL TCGF. The amino acid sequence of Jurkat TCGF, which has been confirmed directly by sequence analysis of the protein, is underlined. The site of cleavage of the signal peptide (residues S1–S20) (↓) was deduced from the sequence of the NH_2 terminus of the purified proteins. The experimentally determined amino acid sequence used to synthesize one of the oligonucleotide probes is indicated by hatch marks.

containing 50% Formamide, 3× NaCl/Cit, 5× PM, salmon sperm DNA at 100 μg/ml, 0.1% $NaDodSO_4$, and 10% dextran sulfate. The sheet was then washed repeatedly with 1× NaCl/Cit/0.1% $NaDodSO_4$ at 65°C, air-dried, and exposed to Kodak film using intensifying screens. For RNA blotting, poly(A)$^+$ RNA was denatured, electrophoresed in a 6% formaldehyde/1% agarose gel, and transferred to a sheet of GeneScreen (New England Nuclear) by electroblotting. Hybridization with a labeled cloned TCGF DNA probe was carried out as described above in a mixture containing 50% Formamide, 5× NaCl/Cit, 0.05 M sodium phosphate (pH 7), yeast RNA at 100 μg/ml, salmon sperm DNA at 20 μg/ml, 0.1% $NaDodSO_4$, and 10% dextran sulfate.

RESULTS

Partial Amino Acid Sequence of Human TCGF. The NH_2-terminal amino acid sequence of the purified intact protein identified alanine as the NH_2-terminal residue of both PBL and Jurkat TCGF, and there was no difference between the two molecules in the sequence of the first 15 residues (Table 1). The amino acid at position 3 could not be identified for either protein because of a chemical modification of this residue. This amino acid for Jurkat TCGF has recently been reported to be an *N*-acetyl-D-galactosamine-modified threonine (29). The more detailed sequence of Jurkat TCGF obtained by sequence analysis of endopeptidase-Lys C-generated peptides is summarized in Table 1. In addition, the COOH terminus of Jurkat TCGF was determined to be Leu-Thr by analysis of the first two residues released by treatment of the intact protein with carboxypeptidase A (Table 1).

Cloning the Human TCGF Sequence from Normal PBL mRNA. A mixture of eight 14-mer oligonucleotides corresponding to a portion of the Jurkat TCGF amino acid sequence (Lys-Phe-Tyr-Met-Pro; Table 1) was synthesized. An effort to identify TCGF clones in a cDNA library from stimulated PBL mRNA using this probe was in progress when Taniguchi *et al.* (14) presented the complete DNA sequence of a Jurkat cDNA clone. As their DNA sequence was entirely consistent with our amino acid sequence data (see below), the alternative strategy of synthesizing two exact oligonucleotide probes was adopted. One of these probes (G-C-A-C-C-T-A-C-T-T-C-A-A-G-T-T-C) encodes the NH_2 terminus of mature TCGF, a region where the two proteins are known to have identical sequence (see above). The second probe (C-T-G-A-T-T-A-A-G-T-C-C-C-T-G-G-G) is complementary to Jurkat TCGF mRNA in the middle of the protein coding region. Screening of 40,000 cDNA clones identified six colonies that hybridized to both 17 mers. Five of these clones had inserts of 800–900 base pairs (bp). The entire nucleotide sequence of two clones (pTCGF-5 and pTCGF-11) (Fig. 1) and the partial sequence of a third was determined. The sequence was identical between the clones and was consistent with all of our amino acid sequence information (Fig. 1).

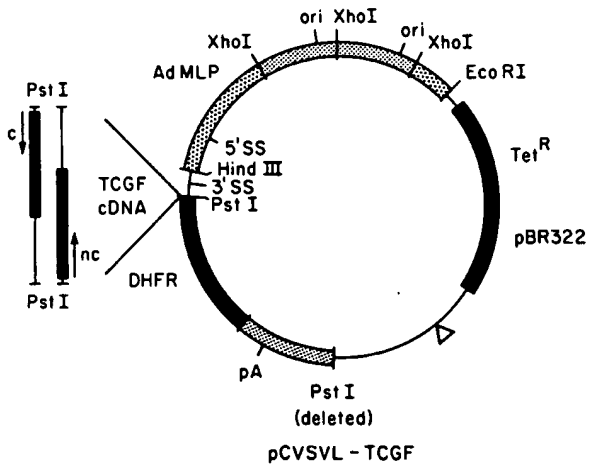

FIG. 2. Plasmid constructed for expression of TCGF in COS-7 cells. pCVSCL-$TCGF_c$ carries the TCGF coding strand downstream from the adenovirus major late promoter while pCVSVL-$TCGF_{nc}$ has the insert fragment in the opposite orientation. The control elements in pCVSVL (19) include the adenovirus late promoter (Ad MLP) and 5′ splice site (5′ SS), a 3′ splice site from a mouse immunoglobulin gene (3′ SS), the polyadenylylation site from the simian virus 40 early region (pA), a duplicated simian virus 40 origin of replication (SV40 ori), and a deletion in pBR322 that enhances replication of such plasmids in animal cells (30). Selectable genes in the vector are those for tetracycline resistance (Tet^R) and mouse dihydrofolate reductase (DHFR).

To confirm that the PBL cDNA we had isolated encoded biologically active TCGF, a cDNA insert of 800 bp from one of the clones (pTCGF-11) with 17 bp of 5′ untranslated sequence and 250 bp of 3′ untranslated sequence was ligated directly into *Pst*-linearized expression vector pCVSVL. The DNAs of the two resulting plasmids, one with the correct orientation (pCVSVL-$TCGF_c$) and the other with the reverse polarity (pCVSVL-$TCGF_{nc}$) with respect to the adenovirus late promoter (Fig. 2), were introduced into COS-7 cells. Assays of supernatants and cellular extracts prepared 48 hr later showed that the production of TCGF activity by COS-7 cells was totally dependent on transfection by pCVSVL-$TCGF_c$ DNA; no activity was detected for cells transfected with pCVSVL-$TCGF_{nc}$ DNA (Table 2). Also, the cell division of TCGF-dependent mouse CTLL cells was completely dependent on conditioned medium from the COS-7 cells transfected with pCVSVL-$TCGF_c$ DNA (Table 2).

Organization of the TCGF Gene. The structural organization of the TCGF gene in normal PBL was examined by the Southern blot procedure (23). Illustrative data are shown in Fig. 3*a*. Each of the following enzymes, which do not cleave within the TCGF cDNA, generate one specific DNA fragment larger than 10 kilobases (kb): *Bam*HI, *Kpn* I, *Sst* I, *Pst* I, and *Pvu* II. *Eco*RI, which also does not cleave within the TCGF cDNA, generated two comigrating TCGF-specific DNA fragments (3.8–4.0 kb) that can be distinguished because one of them contains an internal *Bgl* II site. *Xba* I, which cleaves the cDNA clone once, gives at least three TCGF-specific fragments (about 6.8, 3.8, and 1.04 kb). *Hin*fI and *Mbo* I (data not shown), which each cleave the TCGF cDNA twice, generated at least two (about 0.72 and 0.51 kb) and three (about 2.4, 1.2, and 0.7 kb) fragments, respectively. None of these fragments corresponded to the internal fragments of the cDNA clone.

The organization of the TCGF sequences in cellular DNAs from several different sources was compared by cleaving the DNAs with *Bgl* II, *Eco*RI, and *Xba* I (Fig. 3*b*) and other restriction enzymes (data not shown). The 6 DNAs shown in Fig. 3*b* and more than 20 other DNAs, including those from

Table 2. Expression of TCGF cDNA in COS-7 cells

	TCGF activity, units		T-cell growth
	Cell extract	Conditioned medium	% increase (+) or decrease (−) in cell number
No DNA	0	0	−81
pCVSVL-$TCGF_c$	8	44	+24
pCVSCL-$TCGF_{nc}$	0	0	NT

TCGF activity was determined by measuring thymidine incorporation by mouse CTLL cells (21). One unit is defined as the dilution that gives 50% maximal response with a laboratory TCGF standard. NT, not tested.

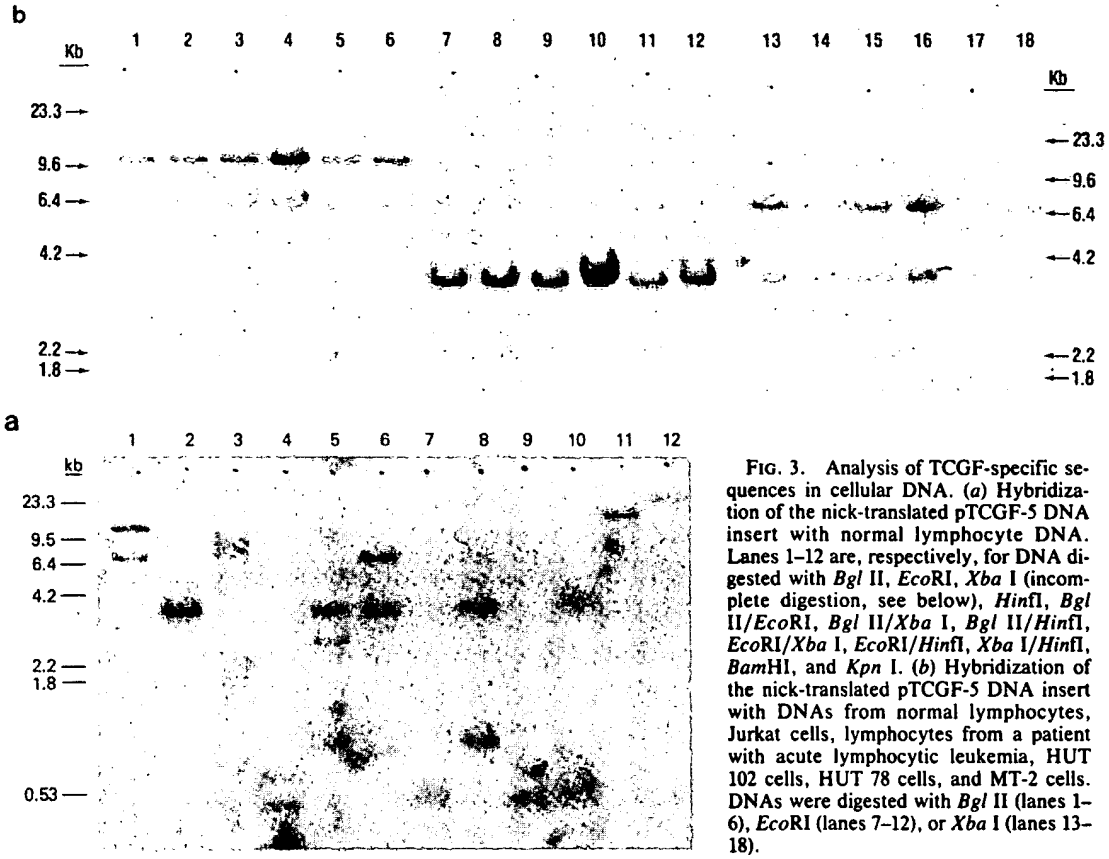

FIG. 3. Analysis of TCGF-specific sequences in cellular DNA. (*a*) Hybridization of the nick-translated pTCGF-5 DNA insert with normal lymphocyte DNA. Lanes 1–12 are, respectively, for DNA digested with *Bgl* II, *Eco*RI, *Xba* I (incomplete digestion, see below), *Hin*fI, *Bgl* II/*Eco*RI, *Bgl* II/*Xba* I, *Bgl* II/*Hin*fI, *Eco*RI/*Xba* I, *Eco*RI/*Hin*fI, *Xba* I/*Hin*fI, *Bam*HI, and *Kpn* I. (*b*) Hybridization of the nick-translated pTCGF-5 DNA insert with DNAs from normal lymphocytes, Jurkat cells, lymphocytes from a patient with acute lymphocytic leukemia, HUT 102 cells, HUT 78 cells, and MT-2 cells. DNAs were digested with *Bgl* II (lanes 1–6), *Eco*RI (lanes 7–12), or *Xba* I (lanes 13–18).

normal, uninfected, and HTLV-infected leukemic cells and cells from patients with autoimmune deficiency syndrome, gave identical restriction patterns.

Specific Expression of TCGF mRNA. To examine the level of regulation of synthesis of TCGF, poly(A)$^+$ RNA from several TCGF-producer and -non-producer cells was analyzed by the RNA blot procedure (Fig. 4). A human TCGF-specific messenger of approximately 900 nucleotides (11S) was readily detected in mRNA isolated from stimulated PBL and Jurkat cells. The corresponding mRNA from gibbon lymphosarcoma cells (MLA 144) was approximately 1100 nucleotides long (13–14S). We observed only one species of TCGF mRNA in each positive RNA preparation even under relaxed hybridization conditions (4× NaCl/Cit at 45°C; data not shown). A specific TCGF mRNA could not be detected in RNA samples from unstimulated PBL, unstimulated Jur-

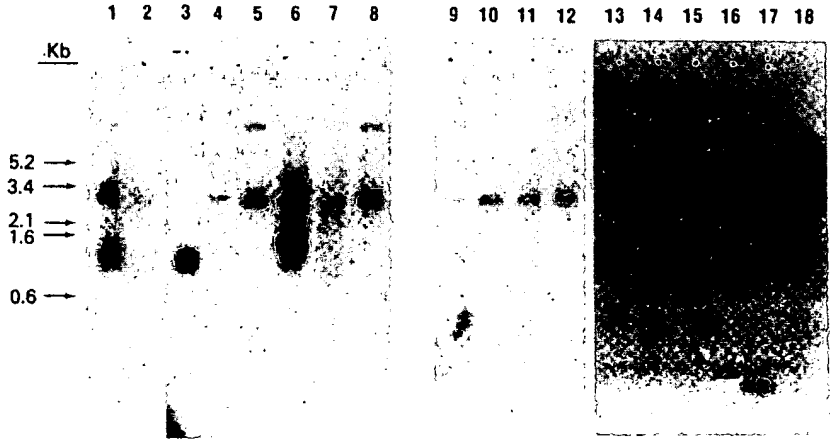

FIG. 4. Analysis of cellular RNA for TCGF-specific mRNA. Hybridization of the nick-translated pTCGF-11 DNA or pTCGF-5 DNA insert to cellular RNAs. Lanes 1–12 are, respectively, for phytohemagglutinin (PHA)-stimulated lymphocytes, unstimulated lymphocytes, PHA/phorbol myristate acetate-stimulated Jurkat cells, unstimulated Jurkat cells, 6G1 cells, MLA 144 cells, Molt-4 cells, HL-60 cells, Daudi cells, Raji cells, trophoblast 3A cells, and SD cells. TCGF-specific RNA appears as a 900-nucleotide band (1100 nucleotides for MLA 144 cells). The 2300-nucleotide band resulted from hybridization of a trace contaminating sequence in the pTCGF-11 (but not in the pTCGF-5) probe to an abundant mRNA species (data not shown) that is constitutively expressed in many cell types examined. Lanes 13–18 show the kinetics of induction in Jurkat cells, and these are, respectively, for RNA isolated 0, 2, 4, 6, 8, and 24 hr after induction.

kat cells, gibbon 6G1 cells, or the human cells Molt-4 (immature T cell), CCRF-CEM (immature T cell), HL-60 (myeloid), Daudi (B cell), and Raji (B cell). Molt-4 and CCRF-CEM were also negative even after treatment with phytohemagglutinin and phorbol myristate acetate (data not shown). Since the TCGF probe did not detect a specific RNA in the colony-stimulating factor-producer cell line 3A, TCGF and CSF mRNAs must not be substantially related. Fig. 4 also shows the kinetics of induction of TCGF mRNA in Jurkat cells. TCGF mRNA reached its maximal value 4–6 hr after induction and its level declined noticeably by 24 hr. The extracellular TCGF reaches its maximal level 12–14 hr after induction in these cells (data not shown).

DISCUSSION

The TCGF proteins from normal PBL and leukemic Jurkat cells, purified to homogeneity, show some differences in biochemical properties. These could be due to differences in gene structure or post-translational modifications. The first 15 residues of the amino acid sequences of the two proteins, however, are identical (Table 1). The complete amino acid sequence of Jurkat TCGF, predicted from a cDNA clone, was recently presented (14). The PBL cDNA clones that we analyzed showed identical sequence among themselves, and one of these clones, when inserted into an expression vector, synthesized functional TCGF. Comparison of the nucleotide sequence of PBL TCGF cDNA with that of Jurkat TCGF cDNA shows them to be essentially identical, with 1 nucleotide difference (out of 750) at nucleotide 498 (an adenosine to guanosine change), which does not change the amino acid sequence of the protein and may represent polymorphism among individuals. More recently reported sequence of a cDNA clone for human splenocytes of a single donor also found guanosine at the corresponding position 498 (31). The identity of the Jurkat and the PBL cDNA sequence implies that differences in the two proteins are due to post-translational events.

The partial amino acid sequence of the proteins and the nucleotide sequence of cDNA clones allows the precise definition of some structural features of TCGF. The nucleotide sequence shows that the cDNA clones contain up to 50 nucleotides of 5′ noncoding sequence, approximately 280 nucleotides of 3′ flanking sequence, and 450 nucleotides of coding sequence. Since the amino terminus of both PBL and Jurkat TCGF is Ala-Pro (Table 1), TCGF must be processed from a precursor polypeptide with a 20-amino acid residue signal peptide with cleavage occurring between serine and alanine (Fig. 1). Cleavage at similar sites has been observed with other secretory proteins (30) and therefore Tanaguchi *et al.* (14) correctly predicted the cleavage site. Further, since the carboxyl terminus of Jurkat TCGF is Leu-Thr-COOH (Table 1), which is the predicted sequence preceding the termination codon (Fig. 1), there is no proteolytic cleavage at the carboxyl terminus, at least for Jurkat TCGF.

Analysis of the TCGF sequences in genomic DNA strongly suggests that it is a single-copy gene (also stated in ref. 14), although we have not yet rigorously excluded the possibility of more than one copy in tandem. It must also have an intron(s), because digestion of genomic DNA with restriction enzymes that cleave the cDNA more than once gives fragments that are not colinear with the cDNA cleavage fragments. Further, genomic DNAs from a variety of cell types gave identical restriction patterns. We were unable to detect any obvious polymorphism, rearrangement, or amplification of the gene in different cell types, including cells that produce TCGF constitutively or produce it only after induction, or leukemic cells with or without human T-cell leukemia/lymphoma virus infection.

Expression of the TCGF gene was detected as a single 900-nucleotide mRNA species. No other mRNA was detected even under conditions of low-stringency hybridization. The TCGF-specific mRNA was detected only in TCGF-producing cell lines, indicating that, in all cases examined, regulation is at the messenger level.

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Hybridomas by Antigenic Determinant

There are approximately 1,000 hybridomas in the ATCC Cell Biology Collection. They are listed by the antigenic determinant recognized by their expressed monoclonal antibodies. For more information on a hybridoma, see the main list on page 30 or use the catalog number to find the entry in the cell biology section of the ATCC online catalog.

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
Abelson murine leukemia virus, 16-kDa antigen	rat/mouse	IgG2a	CDR1	HB-213
abl oncogene peptide, synthetic	mouse	IgG1 and IgG2b	310-29F7	CRL-2656
abl oncogene peptide, synthetic	mouse	IgG1 and IgG2b	311-3D4	CRL-2657
abl oncogene peptide, synthetic	mouse	IgG1	312-13E8	CRL-2658
Acetylcholine receptor (AChR) alpha subunit	rat	IgG2a	mAb64	HB-8987†
Acetylcholine receptor (AChR) alpha subunit	rat/mouse	IgG1	mAb 35	HB-8857†
Acetylcholine receptor (AChR) alpha subunit	rat/mouse	IgG1	mAb35	TIB-175
Acetylcholine receptor, neuronal, chicken	rat/mouse	IgG2a	mAb 270	HB-189
Acetylcholine receptor, neuronal, rat	rat/mouse	IgG2a	mAb 270	HB-189
Acetylcholinesterase, human	mouse	IgG1	AE-1	HB-72
Acetylcholinesterase, human	mouse	IgG1	AE-2	HB-73
Acid phosphatase, prostatic (PAP), human	mouse	IgG1	RLTM01	HB-8526†
Acid phosphatase, prostatic (PAP), human	mouse	IgG1	RLTM02	HB-8523†
Actin	mouse	IgG1	ACT I	HB-80
Actin	mouse	IgG1	ACT IV	HB-81
Actinin, alpha	mouse	IgM	G-3-5	CRL-2252
Addressin, mucosal vascular, mouse	rat/mouse	IgG2a	MECA-89	HB-292
Addressin, peripheral node, mouse	rat/mouse	IgM	MECA-79	HB-9479†
Adenocarcinoma, colon, human	mouse	IgG1	CLT 85	HB-8240†
Adenocarcinoma, colon, human	mouse	IgG3	HT 29/36	HB-8248†
Adenovirus group-specific antigen	mouse	IgG2a	2Hx-2	HB-8117†
Agrobacterium tumefaciens biovar 3	mouse	IgG1	F21-1D3G7C8	HB-9463†
Aldosterone	mouse	IgG1	A2E11	CRL-1846
Alpha fetoprotein (AFP), human	mouse	IgG1; kappa	OM 3-1.1	HB-134
Alpha-1,3-dextran	mouse	IgA; lambda	J558	TIB-6
Alveolar surfactant protein (ASP)	mouse	IgG	DS-1	HB-8906†
Alveolar surfactant protein (ASP)	mouse	IgG1	DS-3	HB-8651†
Alveolar surfactant protein (ASP)	mouse	IgG1	DS-5	HB-8653†
Alveolar surfactant protein (ASP)	mouse	IgG1	DS-6	HB-8652†
Amylase, salivary, human	mouse	IgG2a	110-5	HB-8984†
Angiotensin-converting enzyme (ACE)	mouse	IgM	α-ACE 3.1.1	HB-8191†
Annexin I, human	mouse	IgG1	EH17a	CRL-2209
Annexin I, human	mouse	IgG1	EH7a	CRL-2194
Annexin II, human	mouse	IgG1	EH7a	CRL-2194
Antigen-dependent killer (K) cells, human	mouse	IgM; kappa	HNK-1	TIB-200
AP-2 adaptor protein of clathrin coated vesicles	mouse	IgG1	AP.6	CRL-2227
Apolipoprotein A-I (Apo-A-I), human	mouse	IgG1	A5.4	CRL-2275
Apolipoprotein E (ApoE), human	mouse	IgG1	WU E-14	CRL-2255
Apolipoprotein E (ApoE), human	mouse	IgG1	WU E-4	CRL-2247
Asialo GM1	mouse	IgM	SH-34	CRL-2405
Asialo GM2	mouse	IgM	2D4	TIB-185
Astrocyte protein, human	mouse	IgM	J1-31	CRL-2253
Astrocyte, rat	mouse	IgG2a	RAN-2	TIB-119
Astrocytoma cell line, human	mouse	IgG2a	G253	HB-9706†
Astrocytoma cell line, human	mouse	IgG1	K117	HB-8553†
Astrocytoma cell line, human	mouse	IgG1	S5	HB-9255†
Astrovirus group antigen	mouse	IgG1	7F2-6D4-8E7	HB-11945†

* Part of the NBL collection; see page12. † Patent item; see page 12.
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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
ATPase, rat (Na, K dependent)	mouse	IgG1	9-A5	CRL-1844
ATPase, rat (Na, K dependent)	mouse	IgG1	9-B1	CRL-1845
Autocrine growth factor, 15 kDa, human	mouse	IgM	CBL-1	HB-8214†
B cell antigen (p50), mouse	rat/mouse	IgM	RA3-2C2/1	TIB-145
B cell derived malignancies, human	mouse	IgG2a	Lym-1	HB-8612†
B cell growth factor 1, mouse	rat/mouse	IgG1	11B11	HB-188
B cell precursors, mouse	rat/mouse	IgG2b	14.8	TIB-164
B cell stimulatory factor 1, mouse	rat/mouse	IgG1	11B11	HB-188
B cells, bovine	mouse	IgG2a	CC56	HB-273
B cells, human	mouse	IgG2a	Lym-1	HB-8612†
B lymphocytes, mouse	rat/mouse	IgM	J11d.2	TIB-183
B220, mouse	rat/mouse	IgM	RA3-3A1/6.1	TIB-146
B7.1, mouse	hamster/mouse	IgG	16-10A1	HB-301
B7.1, mouse	rat/mouse	IgG2a	1G10	CRL-2223
B7.2, mouse	rat/mouse	IgG2b	2D10	CRL-2226
B7.2, mouse	rat/mouse	IgG2a	GL1	HB-253
Basal cells (skin), human	mouse	IgG1	VM-2	HB-8530†
BCGF-1, mouse	rat/mouse	IgG1	11B11	HB-188
Bicoid (bcd) protein, *Drosophila melanogaster*	mouse	IgG1	bcd mab23	CRL-2107
Blood group A antigen	human	IgM	HAA1	HB-8534†
Bluetongue virus VP7	mouse	IgG2b	7D3A.2	CRL-1886
Bluetongue virus VP7	mouse	IgG2a	8A3B.6	CRL-1875
Bluetongue virus VP7	mouse	IgG2b	8B1B.1	CRL-1877
Bovine herpesvirus 1 (BHV-1)	bovine/mouse	IgG1	αBL5C2.870005	HB-9907†
Bovine herpesvirus 1 (BHV-1)	bovine/mouse	IgG1	αBL5C2.870009	HB-9908†
Bovine herpesvirus 1 (BHV-1)	bovine/mouse	IgG1	αBL5C2.870016	HB-9909†
Bovine herpesvirus 1 (BHV-1)	mouse	IgG1	1B8-F11	CRL-1852
Bovine herpesvirus 1 (BHV-1)	mouse	IgG2b	2H6-C2	CRL-1853
Bp35 (B cell antigen), human	mouse	IgG2a	1F5	HB-9645†
Bp50 (B cell antigen), human	mouse	IgG1	G28-5	HB-9110†
Breast cancer cells, human	mouse	IgG1	317G5.C1D3	HB-8691†
Breast cancer cells, human	mouse	IgG2a	454C11	HB-8484†
Breast cancer cells, human	mouse	IgG1	520C9	HB-8696†
Breast cancer cells, human	mouse		650E2-2B12	HB-10812†
BSF-1, mouse	rat/mouse	IgG1	11B11	HB-188
Bubonic plague bacillus	mouse	IgA	F1-3G8-1	HB-192
C3d receptor (CR2), human	mouse	IgG2a; kappa	THB-5	HB-135
Calpain 2 (CAPN2), bovine	mouse	IgG1 (kappa)	P-1	CRL-2588
Calpain, human	mouse	IgG1 (kappa)	P-6	CRL-2589
Calpain, human	mouse	IgG1 (kappa)	P-9	CRL-2590
Canine adenovirus type 1 (CAV-1)	mouse	IgG1	2E10-H2	CRL-1812
Canine adenovirus type 2 (CAV-2)	mouse	IgG2a	4H1-A7	CRL-1813
Canine distemper virus (CDV)	mouse	IgG1	CDC 1C42H11	HB-216
Carcinoembryonic antigen (CEA)	mouse	IgM	1116NS-3d	CRL-8019†
Carcinoembryonic antigen (CEA)	mouse	IgG1; kappa	T84.66A3.1A.1F2	HB-8747†
Carcinoma cells, human	mouse	IgG3	KC-4G3	HB-8709†
Carcinoma cells, human	mouse	IgM	KC-4M1	HB-8710†
Carcinoma-associated antigen, heat stable, human	mouse	IgG2a	AS 33	HB-8779†
Calpastatin (CAST), human	mouse	IgG1 (kappa)	PI-11	CRL-2591
C-cadherin	mouse		AA5	CRL-2637
CC chemokine receptor CCR9	mouse	IgG2b	LS129-3C3-E3-1	HB-12653†
CC-chemokine receptor 1 (CCR1), human	mouse	IgG1 (kappa)	LS-125-2D4-11-10-1	HB-12644†
CC-chemokine receptor 2 (CCR2), human	mouse	IgG2a (kappa)	LS132.1D9	HB-12549†
CC-chemokine receptor 2 (CCR2), human	mouse	IgM	LS132.8G2	HB-12550†
Chemokine receptor 4 (CCR4), human	mouse	IgG1 (kappa)	1G1	HB-12624†
CD1, bovine	mouse	IgG2a	CC20	HB-267
CD1, human	mouse	IgG1	OKT 6	CRL-8020†
CD1, pig	mouse	IgG2a; kappa	76-7-4	HB-140
CD1.1, mouse	rat/mouse	IgG2b; kappa	15C6	HB-326
CD1.1, mouse	rat/mouse	IgG2b; kappa	15F7	HB-322
CD1.1, mouse	rat/mouse	IgG2b; kappa	19F8	HB-321

* Part of the NBL collection; see page 12. † Patent item; see page 12.
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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
CD1.1, mouse	rat/mouse	IgG1; kappa	20H2	HB-323
CD1.1, mouse	rat/mouse	IgG2b	4C4	HB-327
CD1w2, bovine	mouse	IgG2a	CC20	HB-267
CD2, bovine	mouse	IgG1	CC42	HB-272
CD2, bovine	mouse	IgG2a	IL-A42	CRL-1870
CD2, human	mouse	IgG2a	35.1	HB-222
CD2, human	mouse	IgG1	OKT 11	CRL-8027†
CD2, human	mouse	IgG1	TS2/18.1.1	HB-195
CD2, sheep	mouse	IgG2a	36F-18C	HB-285
CD3 epsilon chain, human	mouse	IgG2b	BC3	HB-10166†
CD3, human	mouse	IgM	38.1	HB-231
CD3, human	mouse	IgG2a	OKT 3	CRL-8001†
CD3, mouse	hamster/mouse	IgG	145-2C11	CRL-1975
CD4, bovine	mouse	IgG1	CC30	HB-270
CD4, bovine	mouse	IgG2a	CC8	HB-280
CD4, bovine	mouse	IgG2a	IL-A11	CRL-1879
CD4, human	mouse	IgG2b	OKT 4	CRL-8002†
CD4, mouse	rat/mouse	IgG2b	GK1.5	TIB-207
CD4, sheep	mouse	IgG1	17D	HB-262
CD4a, pig	mouse	IgG2b; kappa	74-12-4	HB-147
CD4-binding domain of the gp120 protein of HIV-1	human/mouse	IgG1	448-D	HB-10895†
CD4-binding domain of the gp120 protein of HIV-1	human/mouse	IgG1	558-D	HB-10894†
CD4-binding domain of the gp120 protein of HIV-1	human/mouse	IgG1	559/64-D	HB-10893†
CD5, bovine	mouse	IgG1	CC17	HB-281
CD5, bovine	mouse	IgG1	CC29	HB-269
CD5, human	mouse	IgG1	OKT 1	CRL-8000†
CD6, bovine	mouse	IgG2b	CC38	HB-266
CD6, human	mouse	IgG2a	12.1	HB-228
CD6, human	mouse	IgM	3Pt12B8	HB-8136†
CD7, human	mouse	IgG1; kappa	T3-3A1	HB-2
CD8, bovine	mouse	IgG1	CC58	HB-275
CD8, bovine	mouse	IgG2a	CC63	HB-264
CD8, bovine	mouse	IgG1	IL-A51	CRL-1871
CD8, human	mouse	IgG2a	51.1	HB-230
CD8, human	mouse	IgG2a	OKT 8	CRL-8014†
CD8, human	mouse	IgG1	S6F1	HB-9579†
CD8 alpha 2.2, mouse	mouse	IgM	83-12-5	CRL-1971
CD9, mouse	rat/mouse	IgG2a	KMC8.8	CRL-2212
CD11a, human	mouse	IgG1	TS2/4.1.1	HB-244
CD11a, mouse	rat/mouse	IgG2b	FD441.8	TIB-213
CD11a, mouse	rat/mouse	IgG2a; kappa	M17/4.4.11.9 (new clone of M17/4.2)	TIB-217
CD11a, mouse	rat/mouse	IgG2b; kappa	M17/5.2	TIB-237
CD11b, human	mouse	IgM; kappa	17aba	HB-248
CD11b, human	mouse	IgG2a; kappa	44aacb	HB-249
CD11b, human	mouse	IgG1	LM2/1.6.11	HB-204
CD11b, human	mouse	IgG2b	OKM 1	CRL-8026†
CD11b, mouse	rat/mouse	IgG2b	5C6 Clone 1	CRL-1969
CD11c, mouse	hamster/mouse	IgG	N418	HB-224
CD14, human	mouse	IgG2b; kappa	26ic	HB-246
CD14, human	mouse	IgG2b	3C10	TIB-228
CD14, human	mouse	IgG1; kappa	60bca	HB-247
CD18, human	mouse	IgG2a; kappa	IB4	HB-10164†
CD18, human	mouse	IgG1	TS1/18.1.2.11	HB-203
CD18, mouse	hamster/mouse	IgG	2E6	HB-226
CD18, mouse	rat/mouse	IgG2a; kappa	M18/2.a.12.7 (new clone of M18/2.a.8)	TIB-218
CD19, mouse	rat/mouse	IgG2a; kappa	1D3	HB-305
CD20, human	mouse	IgG2a	1F5	HB-9645†
CD20, human	mouse	IgG1	C273	HB-9303†
CD21, bovine	mouse	IgG2b	CC51	HB-271

* Part of the NBL collection; see page 12. † Patent item; see page 12.
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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
CD21, human	mouse	IgG2a; kappa	THB-5	HB-135
CD25, human	mouse	IgG2a	7G7B6	HB-8784†
CD25, mouse	rat/mouse	IgM; kappa	7D4	CRL-1698
CD25, mouse	rat/mouse	IgG1	PC 61 5.3	TIB-222
CD28 receptor, mouse	hamster/mouse	IgG	PV1	HB-12352†
CD29, human	mouse	IgG1	TS2/16.2.1	HB-243
CD29, mouse	rat/mouse	IgG2a	KMI6	CRL-2179
CD29, sheep	mouse	IgG1	FW4-101-1-1	HB-289
CD32, human	mouse	IgG2b	IV.3	HB-217
CD32, mouse	rat/mouse	IgG2b	2.4G2	HB-197
CD33, human	mouse	IgG2a	M195	HB-10306†
CD34, human	mouse	IgG1; kappa	AC133.1	HB-12346†
CD35, human	mouse	IgG1; kappa	Mab 543	HB-8592†
CD38, human	mouse	IgG1	OKT 10	CRL-8022
CD38, human	mouse	IgG1	THB-7	HB-136
CD40 ligand (CD154, CD40L), human	mouse	IgG1	hCD40L-M90	HB-12055†
CD40 ligand (CD154, CD40L), human	mouse	IgG1	hCD40L-M91	HB-12056†
CD40 ligand, human	mouse	IgG2a	5c8	HB-10916†
CD40 ligand, mouse	hamster/mouse	IgG	MR1	CRL-2580
CD40, human	mouse	IgG2b	3A8	HB-12024†
CD40, human	mouse	IgG1	G28-5	HB-9110†
CD44, human	mouse	IgG2a	Hermes-3	HB-9480†
CD44, mouse	rat/mouse	IgG1	KM114	TIB-242
CD44, mouse	rat/mouse	IgG1	KM201	TIB-240
CD44, mouse	rat/mouse	IgG2a	KM703	CRL-1896
CD44, mouse	rat/mouse	IgG2a	KM81	TIB-241
CD44, mouse	rat/mouse	IgG2a	LYK-12	HB-316
CD44, mouse	rat/mouse	IgG2a	LYK-16	HB-319
CD44, mouse	rat/mouse	IgG1	LYK-5	HB-310
CD44, mouse, isoforms expressing variable exon V10	rat/mouse	IgG1	LYK-1	HB-306
CD44, mouse, isoforms expressing variable exon V10	rat/mouse	IgG1	LYK-7	HB-311
CD44, mouse, isoforms expressing variable exon V10	rat/mouse	IgG2a	LYK-8	HB-312
CD44, mouse, isoforms expressing variable exon V10	rat/mouse	IgG2a	LYK-9	HB-313
CD44, v4 variant, human	mouse	IgG2a	FW11-10-3	HB-257
CD44, v6 variant, human	mouse	IgG2a	FW11-9-2	HB-256
CD44, v9 variant, human	mouse	IgG1	FW11-24-17-36	HB-258
CD45, human	mouse	IgG2a	4B2	HB-196
CD45, human	mouse	IgG2a	9.4	HB-10508†
CD45, human	mouse	IgG2a; kappa	GAP 8.3	HB-12
CD45, mouse	rat/mouse	IgG2b	M1/89.18.7.HK	TIB-124
CD45, mouse	rat/mouse	IgG2a	M1/9.3.4.HL.2	TIB-122
CD45, mouse	rat/mouse	IgG2a	MB23G2	HB-220
CD45, mouse	rat/mouse	IgG2a	MB4B4	HB-223
CD45, pig	mouse	IgM; kappa	74-9-3	HB-156
CD45R, mouse	rat/mouse	IgM	RA3-3A1/6.1	TIB-146
CD45RA, mouse	rat/mouse	IgG2b	14.8	TIB-164
CD45RC, mouse	rat/mouse	IgM	I/24.D6	HB-251
CD47, human	mouse	IgG1	B6H12.2	HB-9771
CD49a, human	mouse	IgG1	TS2/7.1.1	HB-245
CD49d, sheep	mouse	IgG2b	FW3-218-1	HB-261
CD54, mouse	rat/mouse	IgG2a	BE29G1	HB-233
CD57, human	mouse	IgM; kappa	HNK-1	TIB-200
CD58, human	mouse	IgG1	TS2/9.1.4.3	HB-205
CD62E, human	mouse	IgG2a; kappa	CL2	CRL-2514
CD62E, human	mouse	IgG1; kappa	CL3	CRL-2515
CD62E, human	mouse	IgG1; kappa	CL37	CRL-2516
CD62E, human	mouse	IgG2a	H18/7	HB-11684†

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
CD62L, human	mouse	IgG2a	1H3	HB-284
CD62L, human	mouse	IgG1	DREG200	HB-302
CD62L, human	mouse	IgG1	DREG56	HB-300
CD62L, mouse	rat/mouse	IgG2a	MEL-14	HB-132
CD62L, sheep and bovine	mouse	IgG1	DU1-29	HB-263
CD62P, human	mouse	IgG1	WAPS 12.2	HB-299
CD80, mouse	hamster/mouse	IgG	16-10A1	HB-301
CD117, human	mouse	IgG2a	BA7.3C.9	HB-10716†
CDw128, human	mouse	IgG2a	10H2.12.1	HB-11494†
CDw128, human	mouse	IgG2a	4D1.5.7	HB-11495†
CD151, human	mouse	IgG1	41-2	CRL-2695
CD151, human	mouse	IgG1	50-6	CRL-2696
CD152, mouse	hamster/mouse	IgG	UC10-4F10-11	HB-304
CD154, human	mouse	IgG2a	5c8	HB-10916†
CD154, mouse	hamster/mouse	IgG	MR1	CRL-2580
Cell surface antigen on bovine periodontal ligament cells	mouse	IgM	PDL-1	CRL-1882
Cell surface antigen on human myeloma cells (M-8 antigen system)	mouse	IgG1	D 14	HB-8439†
Centromere protein B (CENP-B), human	mouse	IgG1	2D-7	HB-9667†
Cervical carcinoma, human	human	IgG1; kappa	CLN H11.4	HB-8307†
Cervical carcinoma, human	human	IgM	CLNH5.5	HB-8206†
Channel catfish immunoglobulin	mouse	IgG1; kappa	E-8	HB-10179†
Chlamydia genus-specific antigen	mouse	IgG2b; kappa	89MS30	HB-11300†
Cholesterol	mouse	IgM	2C5-6	HB-8995†
Choriocarcinoma tumor cell antigen, human	mouse	IgG2a	K66	HB-8767†
Choriocarcinoma tumor cell antigen, human	mouse	IgG1	SV63	HB-8766†
Choriocarcinomas, human	mouse	IgG1 (Igh-4a allotype)	162-46.2	HB-187
Chronic lymphocytic leukemia (CLL)	mouse	IgG1	Lym-2	HB-8613†
Class II antigen, beta chain, mouse	hamster/mouse	IgG	KL277	CRL-2030
Class II antigen, beta chain, mouse	mouse	IgG1	KL295	CRL-1996
Class II antigen, beta chain, mouse	mouse	IgG2b	KL304	CRL-2027
Clathrin, bovine (brain)	mouse	IgM	CVC.4	TIB-137
Clathrin, heavy chain, human	mouse	IgG1	TD.1	CRL-2232
Clathrin, heavy chain, human	mouse	IgG1	X22	CRL-2228
Clathrin, light chain, bovine (brain)	mouse	IgG1	CVC.1	TIB-135
Clathrin, light chain, bovine (brain)	mouse	IgG2a	CVC.7	TIB-138
Clathrin, light chain, human	mouse	IgG2b	CON.1	CRL-2229
Colchicine	mouse	IgG2a	C44	CRL-1943
Collagen, bone type 1	mouse	IgG1	1H11	HB-10611†
Colon carcinoma-associated antigens (CCAA), human	mouse	IgG1; kappa	PCA 31.1	HB-12314†
Colon carcinoma-associated antigens (CCAA), human	mouse	IgG2a; kappa	PCA 33.28	HB-12315†
Colon cells, 29-kDa glycoprotein, human	mouse	IgG2a	HT 29/26	HB-8247†
Colon tumor-associated antigen (CTAA) 16.88	human	IgG3; kappa	CO 88BV59-1	CRL-10624†
Colon, adenocarcinoma, human	mouse	IgG1	CLT 85	HB-8240†
Colon, adenocarcinoma, human	mouse	IgG3	HT 29/36	HB-8248†
Colonic mucin glycoprotein, human	mouse	IgG2a	UC7	HB-9753†
Colonic protein, human	mouse	IgM	7E12H12	HB-9397†
Colony stimulating factor, subclass I (CSF-I), human	mouse	IgG1	F18 AF1	HB-8208†
Colony stimulating factor, subclass I (CSF-I), human	mouse	IgG1	F1A3-23	HB-8207†
Colorectal carcinoma monosialoganglioside	mouse	IgG1	1116-NS-19-9	HB-8059†
Colorectal carcinoma-associated tumor antigen	mouse	IgG2b	XMMCO-791	HB-9173†
Common leukocyte antigen, human	mouse	IgG2a	4B2	HB-196
Common leukocyte antigen, mouse	rat/mouse	IgG2b	M1/89.18.7.HK	TIB-124
Common leukocyte antigen, mouse	rat/mouse	IgG2a	M1/9.3.4.HL.2	TIB-122
Common leukocyte antigen, mouse	rat/mouse	IgG2a	MB23G2	HB-220
Common leukocyte antigen, mouse	rat/mouse	IgG2a	MB4B4	HB-223
Complement C1q, human	mouse	IgG	12A5B7	HB-8328†
Complement C1q, human	mouse	IgG	4A4B11	HB-8327†

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
Complement C3b receptor, human	mouse	IgG1; kappa	Mab 543	HB-8592†
Concanavalin A (Con A)	mouse	IgG1	71A7	TIB-147
Cortical thymic epithelium, mouse	rat/mouse	IgG2a	CDR1	HB-213
Cortical thymocytes, mouse	rat/mouse	IgM	J11d.2	TIB-183
Coxsackievirus B4	mouse	IgG2a; kappa	204-4	HB-185
Coxsackievirus B4	mouse	IgG2a; kappa	339-1	HB-186
Coxsackievirus B4	mouse	IgG2a; kappa	356-1	HB-181
Coxsackievirus B4	mouse	IgG2a; kappa	38-1	HB-182
Coxsackievirus-adenovirus receptor (CAR), human	mouse	IgG1	RmcB	CRL-2379
CR1, human	mouse	IgG1; kappa	Mab 543	HB-8592†
C-reactive protein, human	mouse	IgG2a; kappa	HD2-4	HB-86
Creatine kinase - MM and MB, human	rat/mouse	IgG2a; kappa	CKMM 14.15	HB-9419†
Creatine kinase - MM, human	rat/mouse	IgA; kappa	CKMM 14.5	HB-9420†
Creatine kinase - MM, human	rat/mouse	IgG1; kappa	CKMM 14.52	HB-9421†
CTLA-4, mouse	hamster/mouse	IgG	UC10-4F10-11	HB-304
Cutaneous lymphocyte antigen (CLA), human	rat/mouse	IgM	HECA-452	HB-11485†
Cutaneous melanocytes (M-10 antigen system), human	mouse	IgG1	M 144	HB-8440†
Cutaneous melanocytes (M-24 antigen system), human	mouse	IgG1	M-24 (M138)	HB-8449†
Cutaneous melanocytes (M-25 antigen system), human	mouse	IgG2b	L368	HB-8450†
Cutaneous melanocytes (M-4 antigen system), human	mouse	IgG1	M 111	HB-8438†
CXCR3	mouse	IgG1 (kappa)	1C6	HB-12330†
Cystic fibrosis transmembrane conductance regulator (CFTR)	mouse	IgG1	mAb 13-1	HB-10565†
Cystic fibrosis transmembrane conductance regulator (CFTR)	mouse	IgG2a; kappa	mAB 24-1	HB-11947†
Cystic fibrosis transmembrane conductance regulator (CFTR)	mouse	IgG1; kappa	mAB 24-2	HB-11946†
Cytokeratin 18 (CK18)	mouse	IgG	UCD/PR 10.11	HB-8694†
Cytokeratin 8 (CK8)	mouse	IgG	UCD/PR 10.11	HB-8694†
Cytomegalovirus (HCMV) UL18 heavy chain, human	mouse	IgG1	10C7	CRL-2430
Cytomegalovirus (HCMV), immediate - early antigen, human	mouse	IgG1	L-14	HB-8554†
Cytomegalovirus (MCMV) m144 heavy chain, mouse	mouse	IgG1	15C6	CRL-2431
DEC-205, human	mouse	IgG2b	MG38	CRL-2640
DEC-205, mouse	rat/mouse	IgG2a	DEC-205	HB-290
Delta heavy chain, human	mouse	IgG3; kappa	δTA4-1	HB-70
Dendritic cell antigen, human	mouse	IgG2b	MG38	CRL-2640
Dendritic cell antigen, mouse	rat/mouse	IgG2a	DEC-205	HB-290
Dendritic cells, mouse	rat/mouse	IgG2b	33D1	TIB-227
Dengue virus complex	mouse	IgG2a	D3-2H2-9-21	HB-114
Dengue virus type 1	mouse	IgG1	15F3-1	HB-47
Dengue virus type 3	mouse	IgG1	5D4-11	HB-49
Dengue virus type 4	mouse	IgG1	1H10-6	HB-48
Dengue virus-2, type specific determinant	mouse	IgG1	3H5-1	HB-46
Dinitrophenyl (DNP)	hamster/mouse	IgG	UC8-1B9	CRL-1968
Dioxins	mouse	IgG2a; kappa	DD-4	HB-9743†
Diphtheria toxin	human/mouse	IgG	16M3F10	HB-8363†
Disialosyl Lea (tumor associated fucoganglioside)	mouse	IgG3	FHCR-1-2516/FH7	HB-8861†
DNA (single stranded)	mouse	IgG3	MRSS-1 (D_2D_4)	HB-69
DNA polymerase alpha, human	mouse	IgG1	SJK-132-20	CRL-1640
DNA polymerase alpha, human	mouse	IgG1	SJK-237-71	CRL-1645
DNA polymerase alpha, human	mouse	IgG1	SJK-287-38	CRL-1644
DNA polymerase alpha, human	mouse	IgG1	STK 1	CRL-1652
DNA polymerase epsilon (pol epsilon), human	mouse	IgG2a	3C5.1	CRL-2284
DNA polymerase III holoenzyme, *Escherichia coli*	mouse	IgM	123-10	CRL-1707
DNA polymerase III holoenzyme, *Escherichia coli*	mouse	IgG1	123-28	CRL-1713

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
DNA polymerase III holoenzyme, *Escherichia coli*	mouse	IgM	68-1-2	CRL-1712
DNA, double stranded	mouse	IgM	CH26-1352	HB-8329†
DNP and TNP substituted proteins	mouse	IgA; lambda 2	MOPC 315	TIB-23
EGF receptor	mouse	IgG1	225	HB-8508†
EGF receptor	mouse	IgG1	455	HB-8507†
EGF receptor	mouse	IgG2a	528	HB-8509†
EGF receptor	mouse	IgG	579	HB-8506†
EGF receptor, human	mouse	IgM	Mab 96	HB-9763†
Eimeria tenella sporozoites	mouse	IgG1	S1E4	HB-8332†
Eimeria tenella sporozoites	mouse	IgG2a	S3D3	HB-8331†
Eimeria tenella sporozoites and merozoites	mouse	IgG1	13.90.2	HB-8337†
Eimeria tenella sporozoites and merozoites	mouse	IgG2a	2.03.7	HB-8389†
ELAM-1, human	mouse	IgG2a; kappa	CL2	CRL-2514
ELAM-1, human	mouse	IgG1; kappa	CL3	CRL-2515
ELAM-1, human	mouse	IgG1; kappa	CL37	CRL-2516
ELAM-1, human	mouse	IgG2a	H18/7	HB-11684†
EM10	mouse	IgM; kappa	SM27-1045	HB-11917†
Endothelial cells, IL-1 activated, human	mouse	IgG1	7A9	HB-10135†
Endothelial cells, peripheral lymph node, mouse	rat/mouse	IgM	MECA-79	HB-9479†
Endothelial leukocyte adhesion molecule 1 (ELAM-1), human	mouse	IgG2a; kappa	CL2	CRL-2514
Endothelial leukocyte adhesion molecule 1 (ELAM-1), human	mouse	IgG1; kappa	CL3	CRL-2515
Endothelial leukocyte adhesion molecule 1 (ELAM-1), human	mouse	IgG1; kappa	CL37	CRL-2516
Endothelial leukocyte adhesion molecule 1 (ELAM-1), human	mouse	IgG2a	H18/7	HB-11684†
Endothelium, human	mouse	IgG1; kappa	10B9	HB-172
Endothelium, human	mouse	IgG1; kappa	14E5	HB-174
Ependymal cell, rat	mouse	IgG2a	RAN-2	TIB-119
Epidermal growth factor (EGF) receptor	mouse	IgG1	225	HB-8508†
Epidermal growth factor (EGF) receptor	mouse	IgG1	455	HB-8507†
Epidermal growth factor (EGF) receptor	mouse	IgG2a	528	HB-8509†
Epidermal growth factor (EGF) receptor	mouse	IgG	579	HB-8506†
Epidermal growth factor (EGF) receptor, human	mouse	IgM	Mab 96	HB-9763†
Epidermis, basal layer, fetal and neonatal, human	mouse	IgG1	DAL K20	CRL-2288
Epidermis, basal layer, fetal and neonatal, human	mouse	IgG1	DAL K29	CRL-2291
Epithelial cells, gastrointestinal tract mucosa, 52-kDa protein, human	mouse	IgG1	CLT 152	HB-8244†
Epithelium, human	mouse	IgM; kappa	Ep-16	HB-155
Epstein-Barr virus (EBV)	mouse	IgG1	72A1	HB-168
Epstein-Barr virus (EBV) receptor	mouse	IgG2a; kappa	THB-5	HB-135
Equine infectious anemia virus (EIAV) core antigen (p26)	mouse	IgG1	EIAV 12E8.1	HB-8917†
erb B (v-*erb* B) oncogene peptide, synthetic	mouse	IgG1	171-11B9	CRL-2661
erb B (v-*erb* B) oncogene peptide, synthetic	mouse	IgG1	172-12A4	CRL-2660
erb B (v-*erb* B) oncogene peptide, synthetic	mouse	IgG1; kappa	173-1C11	CRL-2659
erb B2 (c-*erb* B2) protein, human	mouse	IgG1; kappa	20.3	CRL-2655
erb B-2 protein, human	mouse	IgG1	Ab 21.1	HB-11601†
erb B-2 protein, human	mouse	IgG1	Ab 23.1	HB-11602†
Ergonovine	mouse	IgG2b (kappa)	EN9F10	CRL-2403
Erythrocytes, mouse	rat/mouse	IgM	J11d.2	TIB-183
Erythropoietin	mouse	IgG1	5F12 AD3	HB-8209†
Erythropoietin, human	rat/mouse	IgG2a	BF-11	CRL-8164†
Escherichia coli 0157:H7 strain 932	mouse	IgG2a	4E8C12	HB-10452†
Farnesyltransferase, alpha subunit	mouse	IgG1	IgG-IB7	CRL-2418
Fas antigen, human	mouse	IgG1	huFasM3	HB-11726†
Fas antigen, human	mouse	IgG1	huFasM38	HB-11465†
Fc alpha receptor, human	mouse	IgM	My 43.51	HB-12128†
Fc gamma receptor, high affinity, human	mouse	IgG1; kappa	CT6-1D7	CRL-2438
Fc gamma receptor, mouse	rat/mouse	IgG2b	2.4G2	HB-197

* Part of the NBL collection; see page 12. † Patent item; see page 12.
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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
FcRI, human	mouse	IgG1; kappa	CT6-1D7	CRL-2438
FcRI, human	mouse	IgM	My 43.51	HB-12128†
FcRII, mouse	rat/mouse	IgG2b	2.4G2	HB-197
FcRn heavy chain heterodimers	mouse	IgG1	1G3	CRL-2434
FcRn heavy chain heterodimers	mouse	IgG1	2G3	CRL-2435
Feline leukemia virus (FeLV), p27 protein	mouse	IgG	$24IA_{2-2}E_{10}D_5$	HB-8049†
Fibrin, human	mouse		F45J	HB-9740†
Fibrin, human	mouse	IgG1; kappa	MH1	HB-9739†
Fibrinogen, human	mouse		F45J	HB-9740†
Fibronectin, human	mouse	IgG1	HFN 36.3	CRL-1605
Fibronectin, human	mouse	IgG1	HFN 7.1	CRL-1606
Fibronectin, human	mouse	IgG1	P_3NP/PFn	HB-91
Fibronectin, human, onco-fetal determinant	mouse	IgG1	FHCR-1-2813/FDC-6	HB-9018†
Fimbriae (2134P) of enterotoxigenic *E. coli*	mouse	IgG1	αM346C7C1	HB-11124†
Flavivirus group antigen	mouse	IgG2a	D1-4G2-4-15	HB-112
Flk-1/KDR	rat/mouse	IgG1; kappa	DC101	HB-11534†
Follicle stimulating hormone (FSH) receptor, human	mouse	IgG1	FSHR-18	CRL-2688
Forssman antigen	rat/mouse	IgM	M1/22.25.8.HL	TIB-121
Forssman antigen	rat/mouse	IgM	M1/87.27.7.HLK	TIB-123
fos oncogene peptide, synthetic	mouse	IgG2b; kappa	411-14E10	CRL-2663
fos oncogene peptide, synthetic	mouse	IgG1 and IgG2b	413-15D12	CRL-2653
Fumonisin B1	mouse	IgG1 (kappa)	FB8H3 [Mab8H3]	CRL-2402
Gamma heavy chain, human	mouse	IgG1; kappa	1410 KG7	HB-43
Gamma heavy chain, human	mouse	IgG2b; lambda	C3-124	HB-60
6B Ganglioside (tumor-associated fucoganglioside)	mouse	IgM	FHCR-1-2624/FH6/ FHOT-1-3019	HB-8873†
Ganglioside associated with endocrine cells, human T lymphocytes, and neuronal cells	mouse	IgM; kappa	3G5	CRL-1814
Ganglioside GD2	mouse	IgM	Mab 126	HB-8568†
Gangliosides GD2 and GD3	mouse	IgG2a	ME361S2a	HB-9326†
Gangliosides GM3 and GM4, human	human	IgM; kappa	L612	CRL-10724†
Giardia muris trophozoites	mouse	IgG3; kappa	1A3.1	CRL-1961
Giardia muris trophozoites	mouse	IgG2b; kappa	2B5.3	CRL-1960
Giardia muris trophozoites	mouse	IgG1; kappa	3C7.2	CRL-1959
Glioblastoma, human	mouse	IgM	PI 153/3	TIB-198
Glomalin (soil glycoprotein)	mouse	IgM; kappa	32B11	CRL-2559
Glucocorticoid receptor, mouse and rat	mouse	IgG2b	FIGR	CRL-2173
Glutamic acid decarboxylase (GAD)	mouse	IgG1	GAD-1	HB-184
Glycated serum albumin (glycoalbumin)	mouse	IgG	A717	HB-9596†
Glycolipid antigen	mouse	IgM	A2B5 clone 105	CRL-1520
Glycolipids, di- and trifucosylated type 2 chain	mouse	IgG3	FHCR-1-2075/FH4	HB-8775†
Glycophorin A, type M	mouse	IgG1; kappa	6A7M	HB-8159†
Glycophorin A, type M and type N	mouse	IgG1; kappa	10F7MN	HB-8162†
Glycophorin A, type N	mouse	IgG1; kappa	8A2N	HB-8161†
Glycophorin A, type N	mouse	IgG2a; kappa	NN-4	HB-8473†
Glycophorin A, type N, human	mouse	IgM; kappa	NN-3	HB-8474†
Glycophorin A, type N, human	mouse	IgG1; kappa	NN-5	HB-8476†
Glycophorin, human	mouse	IgG1	G26.4.1C3/86	HB-9893†
Glycoprotein antigen, tumor vascular endothelium	mouse	IgG1	H572	HB-11608†
Glycosphingolipid	mouse	IgM	1B2-1B7	TIB-189
Glycosphingolipid	mouse	IgG3	YI 328-18	HB-9306†
Glycosphingolipid, type II chain H structure	mouse	IgM	BE2	TIB-182
Golgi complex (GCI), rat	mouse	IgG1	6F4C5	CRL-1869
Golgi vesicular transport protein	mouse	IgM	4A6	CRL-1928
Gonadotropin releasing hormone, carboxy terminal	mouse	IgG1	USASK/DSIL-LHRH-A1	HB-9094†
gp120 glycoprotein	mouse	IgG1	S5	HB-9255†
gp39, mouse	hamster/mouse	IgG	MR1	CRL-2580
gp70 envelope antigen (ENV) protein of murine leukemia viruses (MuLV)	mouse	IgG2a	48	CRL-1913
gp70 envelope antigen (ENV) protein of murine leukemia viruses (MuLV)	mouse	IgM	514	CRL-1914

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
gp90 glycoprotein, human	mouse	IgG2a	G253	HB-9706†
GPIIIa, platelet, human	mouse	IgG1	AP-3	HB-242
Granulocyte macrophage colony stimulating factor (GM-CSF), human	rat/mouse	IgG2a	BVD2-21C11.3	HB-9569†
Granulocyte macrophage colony stimulating factor (GM-CSF), human	rat/mouse	IgG2a	BVD2-23B6.4	HB-9568†
Granulocyte, human	mouse	IgG2b	OKM 1	CRL-8026†
Granulocyte, pig	mouse	IgG1; kappa	74-22-15	HB-142
Granulocyte, pig	mouse	IgG2b; kappa	74-22-15A	HB-142.1
Growth hormone (hGH), human	mouse	IgG1; kappa	HGH-B	HB-10596†
H-2 (all haplotypes)	rat/mouse	IgG2a	M1/42.3.9.8.HLK	TIB-126
H-2 b	mouse	IgG1; kappa	B8-24-3	TIB-139
H-2 D b	mouse	IgM; kappa	23A-5-21S	HB-36
H-2 D b	mouse	IgM; kappa	28-11-5S	HB-19
H-2 D d	mouse	IgG2a; kappa	34-2-12S	HB-87
H-2 D d	mouse	IgG2a; kappa	34-4-20S	HB-75
H-2 D d	mouse	IgM	34-4-21S	HB-76
H-2 D d	mouse	IgG2a; kappa	34-5-8S	HB-102
H-2 D k	mouse	IgG2a; kappa	15-5-5S	HB-24
H-2 from non-k haplotype mice	rat	IgG2a	K204	HB-221
H-2 K b	mouse	IgM; kappa	28-13-3S	HB-41
H-2 K b	mouse	IgG2a	AF6-88.5.3	HB-158
H-2 K b	mouse	IgG2b; kappa	Y-3	HB-176
H-2 K b, D b	mouse	IgG2a; kappa	28-8-6S	HB-51
H-2 K d	mouse	IgM	31-3-4S	HB-77
H-2 K d	mouse	IgG2a	SF1-1.1.10	HB-159
H-2 K d, D d	mouse	IgG2a; kappa	34-1-2S	HB-79
H-2 K d, D d	mouse	IgM	34-7-23S	HB-101
H-2 K k	mouse	IgG2a; kappa	16-1-11N	HB-16
H-2 K k	mouse	IgG2a; kappa	16-3-1N	HB-25
H-2 K k	mouse	IgG2a; kappa	16-3-22S	HB-5
H-2 K k	mouse	IgG1	AF3-12.1.3	HB-160
H-2 K k, D k	mouse	IgM; kappa	12-2-2S (clone 5F11)	HB-50
H-2 K k, D k	mouse	IgG2b; kappa	15-1-5P	HB-53
H-2 K k, D k	mouse	IgG2a; kappa	15-3-1S	HB-13
H-2 K k, D k	mouse	IgG2a; kappa	16-1-2N	HB-14
H-2 K k, D k	mouse	IgG2a; kappa	3-83P	HB-20
H-2 K of the k, q, p and r haplotypes	mouse	IgG2a	11-4.1	TIB-95
H7 flagella, *E. coli*	mouse	IgG1	MARC 2B7	CRL-2509
Hassall's bodies, human	mouse	IgM	TE15	HB-206
Hassall's bodies, human	mouse	IgG1	TE16	HB-210
Hassall's bodies, human	mouse	IgM	TE19	HB-211
Hassall's bodies, human	mouse	IgG2a	TE8	HB-212
Heat-stable antigen, mouse	rat/mouse	IgG2b	M1/69.16.11.HL	TIB-125
Heat-stable antigen, mouse	rat/mouse	IgG2c	M1/75.16.4.HLK	TIB-127
HeLa cells	mouse		$1A_3$	HB-8563†
Hematopoietic cells, human	mouse	IgG1	B3/25	CRL-8034†
Hen egg lysozyme (HEL)	mouse	IgG1	Aw3.18.14	CRL-2826
Hepatitis B virus surface antigen (HBsAg)	mouse	IgM	H21F8-1	CRL-8018†
Hepatitis B virus surface antigen (HBsAg)	mouse	IgG1	H25B10	CRL-8017†
Hepatitis B virus surface antigen (HBsAg)	mouse	IgG1	H25B10	CRL-8017A†
Hepatocyte growth factor receptor	mouse	IgG1 (kappa)	1A3.3.13	HB-11894†
Hepatocyte growth factor receptor	mouse	IgG1 (kappa)	5D5.11.6	HB-11895†
HER-2/neu	mouse	IgG1 (kappa)	BD5-2d	HB-9689†
HER-2/neu	mouse	IgG1 (kappa)	NB3	HB-10205†
HER-2/neu	mouse	IgG1 (kappa)	TA-1	HB-10206†
HER-2/neu	mouse	IgM (kappa)	OD-3	HB-10204†
HER2 receptor	mouse	IgG1	A-HER2	CRL-10463†
Herpes simplex virus type 1 (HSV-1) glycoprotein	mouse	IgG2a	52-S	HB-8181†
Herpes simplex virus type 1 (HSV-1) glycoprotein	mouse	IgG2a	53-S	HB-8182†

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
Herpes simplex virus type 1 (HSV-1), immediate early protein (ICP 4)	mouse	IgG2a	58-S	HB-8183†
Herpes simplex virus type 1 (HSV-1), internal capsid protein 8 (ICP 8)	mouse	IgG2a	39-S	HB-8180†
Herpes simplex virus type 1 (HSV-1), nucleocapsid protein (p40)	mouse	IgG1	1D4	HB-8068†
Herpes simplex virus type 2 (HSV-2), nucleocapsid protein (p40)	mouse	IgG1	3E1	HB-8067†
HFE	mouse	IgG1	1C3	CRL-2441
HFE	mouse	IgG1	2A11	CRL-2442
HFE	mouse	IgM; kappa	2A5	CRL-2444
HFE	mouse	IgG1	2B7	CRL-2443
HFE	mouse	IgM; kappa	3A5	CRL-2440
HIV gp41	mouse	IgG1; kappa	MH-SVM25	HB-8871†
HIV p17	mouse	IgG1; kappa	MH-SVM33C9	HB-8975†
HIV p24	mouse	IgG2; kappa	MH-SVM23	HB-8870†
HIV p24	mouse	IgG1; kappa	MH-SVM26	HB-8872†
HIV-1 gp120	mouse	IgG1	46-2	CRL-2186
HIV-1 gp120	mouse	IgG1	46-4	CRL-2178
HIV-1 gp120	mouse	IgG1	46-5	CRL-2184
HIV-1 gp120	mouse	IgG1	55-2	CRL-2155
HIV-1 gp120	mouse	IgG1	55-36	CRL-2153
HIV-1 gp120	mouse	IgG2a	55-6	CRL-2156
HIV-1 gp120	mouse	IgG2a	55-83	CRL-2185
HIV-1 gp120	mouse	IgG1	803-15.6	CRL-2395
HIV-1 p17	mouse	IgG1; kappa	MH-SVM33C9	HB-8975†
HIV-1 p24	mouse	IgG1	31-42-19	HB-9726†
HIV-1 p24	mouse	IgG1	31-90-25	HB-9725†
HLA A2, B17	mouse	IgG1	MA2.1	HB-54
HLA A3	mouse	IgG2a; kappa	GAP A3	HB-122
HLA A3	rat/mouse	IgM	WFL3C6.1	HB-8157†
HLA B27, B7	mouse	IgG2a	B27M1	HB-157
HLA B27, Bw47	mouse	IgM	B27M2	HB-165
HLA B5	mouse	IgG1	4D12	HB-178
HLA B7	mouse	IgG1	BB7.1	HB-56
HLA B7, B40	mouse	IgG1	MB 40.3	HB-105
HLA B7, B40	mouse	IgG1	MB40.2	HB-59
HLA B7, Bw22, B27	mouse	IgG1	ME 1	HB-119
HLA B7,B40	mouse	IgG1	BB7.6	HB-115
HLA Bw6	rat/mouse	IgG2b	SFR8-B6	HB-152
HLA DC1	mouse	IgG2a	G2a.5	HB-110
HLA DC1	mouse	IgG2b	G2b.2	HB-109
HLA DQ	mouse	IgG1; kappa	IVD12	HB-144
HLA DQw1	mouse	IgG1	Genox 3.53	HB-103
HLA DR	mouse	IgG1	Antibody 2.06	HB-104
HLA DR, DP, DQ	mouse	IgG1; kappa	IVA12	HB-145
HLA DR, DQ	mouse	IgG2a	9.3F10	HB-180
HLA DR5	rat/mouse	IgG2b	SFR3-DR5	HB-151
HLA heavy chain	mouse	IgG2a; kappa	171-4	HB-296
HLA-DR alpha chain	mouse	IgG2a	LB3.1	HB-298
HMG-CoA reductase (3-hydroxy-3-methyl-glutaryl Coenzyme A reductase)	mouse	IgG1	A9	CRL-1811
Hog renin	mouse	IgG1	F32 VIII C4	CRL-1653
HTLV-III gp41	mouse	IgG1; kappa	MH-SVM25	HB-8871†
HTLV-III p17	mouse	IgG1; kappa	MH-SVM33C9	HB-8975†
HTLV-III p24	mouse	IgG2; kappa	MH-SVM23	HB-8870†
HTLV-III p24	mouse	IgG1; kappa	MH-SVM26	HB-8872†
Human epidermal growth factor (EGF) receptor	mouse	IgG2a; kappa	Mab 108	HB-9764†
H-Y antigen	mouse	IgM; kappa	12/44	HB-9070†
H-Y antigen	mouse	IgM; kappa	12/49	HB-9071†
I-A	mouse	IgG2a	Y-3P	HB-183

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
I-A b	mouse	IgM	25-5-16S	HB-37
I-A b	mouse	IgM	25-9-3S	HB-38
I-A b	mouse	IgG2a	AF6-120.1.2	HB-163
I-A b and I-A d	mouse	IgG2a; kappa	25-9-17S II	HB-26
I-A b and I-A d	mouse	IgG3	BP107.2.2	TIB-154
I-A b, I-A d	mouse	IgM; kappa	28-16-8S	HB-35
I-A b, I-A d, I-A q, I-E d and I-E k	rat/mouse	IgG2b; kappa	M5/114.15.2	TIB-120
I-A b,d	rat/mouse	IgG2b	B21-2	TIB-229
I-A d	mouse	IgG2a; kappa	34-5-3S	HB-85
I-A d	mouse	IgG2a; kappa	MK-D6	HB-3
I-A k	mouse	IgG2b	11-5.2.1.9	TIB-94
I-A k	mouse	IgM; kappa	26-7-11S	HB-15
I-A k	mouse	IgM	26-8-16S	HB-42
I-A of k, r, f and s haplotypes	mouse	IgG2a	10-3.6.2	TIB-92
I-A of the k, r, f and s haplotypes	mouse	IgG2b	10-2.16	TIB-93
I-A s	mouse	IgG2b	MK-S4	HB-4
Ia, human	mouse	IgG1; kappa	L203	HB-171
Ia, human	mouse	IgG1; kappa	L227	HB-96
Ia, human	mouse	IgG2a	L243	HB-55
I-A, I-E, monomorphic, mouse	hamster/mouse	IgG	N22	HB-225
Ia, rabbit	mouse	IgG2a	2C4	CRL-1760
ICAM-1, canine	mouse	IgG1	CL18/6	CRL-2518
ICAM-1, human	mouse	IgG2a	R6.5.D6.E9.B2	HB-9580†
ICAM-1, mouse	rat	IgG2b	YN1/1.7.4	CRL-1878
ICAM-1, mouse	rat/mouse	IgG2a	BE29G1	HB-233
ICAM-4, rat	mouse	IgG1	127H	HB-11911†
Idiotypic determinant on on anti-chlamydia genus antibody	mouse	IgG1; kappa	91MS441	HB-11301†
Idiotypic determinant on the P3X63Ag8 myeloma	mouse protein	IgG2b; kappa	80 V 5B4	TIB-132
I-E	mouse	IgG2b	Y-17	HB-179
I-E k	mouse	IgG2a; kappa	14-4-4S	HB-32
I-E k	mouse	IgG2a; kappa	17-3-3S	HB-6
Ig-4a allotype on mouse IgG1	mouse	IgG2a	Ig(4a)10.9	HB-146
IgA, human	mouse	IgG1; kappa	CH-EB6	HB-200
IgD, Ig-5a allotype, mouse	mouse	IgG2a	Ig(5a)7.2 (formerly 10-4-22)	TIB-149
IgD, mouse	rat/mouse	IgG2a	11-26c	HB-250
IgE, human	mouse	IgG1; kappa	CIA-E-4.15	HB-235
IgE, human	mouse	IgG1; kappa	CIA-E-7.12	HB-236
IgE, human	mouse	IgG2a; kappa	E5BB3IIA2	HB-121
IgG (Fc), human	mouse	IgG2b	HP6000	CRL-1754
IgG (Fc), human	mouse	IgG2a	HP6017	CRL-1753
IgG (Fc), human	mouse	IgG1	HP6058	CRL-1786
IgG (Fd, F(ab')2, Fab), human	mouse	IgG2a	HP6045	CRL-1757
IgG Fc receptor, human	mouse	IgG2b	IV.3	HB-217
IgG1 (Fc), human	mouse	IgG2b	HP6001	CRL-1755
IgG1 (Fc), rat	mouse	IgG2b	RG11/39.4	TIB-170
IgG2 (Fc), human	mouse	IgG1	HP6002	CRL-1788
IgG2 (Fd), human	mouse	IgG1	HP6014	CRL-1752
IgG2, mouse	rat/mouse	IgG2b; kappa	7D2-1.4.1.5	HB-92
IgG2, mouse	rat/mouse	IgG2a	ED1-19-1-6-5	HB-90
IgG2a (Fab'), rat	mouse	IgG2b	RG9/6.13 HLK	TIB-167
IgG2a (Fc), rat	mouse	IgG2b	RG7/1.30	TIB-173
IgG2a, Ig-1a allotype, mouse	mouse	IgG2a	Ig(1a)8.3 (formerly 20-8.3)	TIB-148
IgG2a, Igh-1b allotype, mouse	mouse	IgM	RDP 45/20	TIB-98
IgG2b (Fc), rat	mouse	IgG2b	RG7/11.1	TIB-174
IgG3 (Fc), human	mouse	IgG1	HP6003	CRL-1756
IgG3 (hinge), human	mouse	IgG1	HP6047	CRL-1774
IgG3 hinge region, human	mouse	IgG1	HP6050	CRL-1768
IgG3, mouse	rat/mouse	IgG1	2E.6	HB-128

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
IgG4 (Fab), human	mouse	IgG2a	HP6020	CRL-1789
IgG4 (Fc), human	mouse	IgG3	HP6023	CRL-1776
IgG4 (Fc), human	mouse	IgG1	HP6025	CRL-1775
Igh-5.3 (IgD b,e)	mouse	IgG1	AF6-122.2.5	HB-199
Igh-5.4 (IgD a)	mouse	IgG2b	AMS 9.1.1.1	HB-161
Igh-5.5 (IgD e)	mouse	IgG2b	AF4-73.3.1	HB-201
Igh-5b (IgD b allotype)	mouse	IgG1	Ig(5b)6.3	TIB-96
Igh-6.6 (IgM b)	mouse	IgG1	AF6-78.25.4	HB-162
IgM (Igh-6.5 allotype), mouse	rat/mouse	IgG1; kappa	Bet-1	HB-100
IgM (lambda), human	mouse	IgG2b; kappa	LP4.4	HB-232
IgM (mu heavy chain), mouse	rat/mouse	IgG2b	331.12	TIB-129
IgM, bovine	mouse	IgG1	IL-A30	CRL-1894
IgM, human	mouse	IgG1	M-2E6	HB-138
IgM, mouse	rat/mouse	IgG1; kappa	Bet-2	HB-88
IgM, pig	mouse	IgG1; kappa	5C9	HB-8371†
IgM, rabbit	mouse	IgG1	NRbM	CRL-1839
IL-1 beta, human	mouse	IgG1; kappa	ILB1-H21	HB-10220†
IL-1 beta, human	mouse	IgG1; kappa	ILB1-H34	HB-10221†
IL-1 beta, human	mouse	IgG1; kappa	ILB1-H6	HB-10219†
IL-1 beta, human	mouse	IgG2b; kappa	ILB1-H67	HB-10222†
IL-1 beta, recombinant, bovine	mouse	IgG1	SA22	CRL-2052
IL-2, mouse	rat/mouse	IgG2a	S4B6-1	HB-10968†
IL-4, mouse	rat/mouse	IgG1	11B11	HB-188
IL-8, human	mouse	IgG1	EL-NC-1S	HB-9647†
IL-12 p40, mouse	rat/mouse	IgG2a	R1-5D9	CRL-2360
IL-12 p40, mouse	rat/mouse	IgG2b	R2-10F6	CRL-2358
IL-12 p75, mouse	rat/mouse	IgG2b	R2-9A5	CRL-2357
IL-12, human	rat/mouse	IgG1	20C2	CRL-2382
IL-15, human	mouse	IgG1	hIL-15-M110	HB-12061†
IL-15, human	mouse	IgG1	hIL-15-M111	HB-12062†
Infectious bovine rhinotracheitis virus (IBRV)	mouse	IgG1	1B8-F11	CRL-1852
Infectious bursal disease (IBD) virus	mouse	IgG2a; kappa	B69	HB-9437†
Infectious bursal disease (IBD) virus	mouse	IgG2a; kappa	R63	HB-9490†
Infectious bursal disease (IBD) virus, serotypes 1 and 2	mouse	IgG1; kappa	B29	HB-9746†
Inflammatory cells, human	mouse	IgG1	MY904	HB-9510†
Influenzavirus A matrix protein (M)	mouse	IgG1	M2-1C6-4R3	HB-64
Influenzavirus A nucleoprotein	mouse	IgG1	46/4	HB-67
Influenzavirus A nucleoprotein	mouse	IgG2a	H16-L10-4R5	HB-65
Influenzavirus hemagglutinin	mouse	IgG2a	73/1	HB-66
Insulin	mouse	IgG2a; kappa	BE3F9	HB-133
Insulin	mouse	IgG1; kappa	CC9C10	HB-123
Insulin	mouse	IgG1; kappa	CE9H9	HB-127
Insulin	mouse	IgG1; kappa	CG7C7	HB-126
Insulin	mouse	IgG2a; kappa	DB9G8	HB-124
Insulin (residues A8-10), human	mouse	IgG1; kappa	AE9D6	HB-125
Insulin receptor, human	mouse	IgG1; kappa	αIR-1	HB-175
Insulin receptor, placental, human	mouse	IgG1	DII 33.1	CRL-1827
Integrin, alpha 1, human	mouse	IgG1	TS2/7.1.1	HB-245
Integrin, alpha 4, sheep	mouse	IgG2b	FW3-218-1	HB-261
Integrin, alpha 4/beta 7, mouse	rat/mouse	IgG2a	DATK32	HB-294
Integrin alpha V, integrin beta 3 (vitronectin receptor), human	mouse	IgG1 (kappa)	10C4.1.3	HB-11029
Integrin, beta 1 subunit, mouse	rat/mouse	IgG2a	KMI6	CRL-2179
Integrin, beta 1, human	mouse	IgG1	TS2/16.2.1	HB-243
Integrin, beta 1, sheep	mouse	IgG1	FW4-101-1-1	HB-289
Integrin, beta 2, mouse	hamster/mouse	IgG	2E6	HB-226
Integrin, beta 3, human	mouse	IgG1	AP-3	HB-242
Integrin, beta 7 Integrin, mouse	rat/mouse	IgG2a	FIB21	HB-295
Integrin, beta 7 Integrin, mouse	rat/mouse	IgG2a	FIB504.64	HB-293
Integrin, leukocyte, mouse	hamster/mouse	IgG	N418	HB-224

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Integrin-associated protein, human	mouse	IgG1	B6H12.2	HB-9771†
Integrin-like cellular adhesion molecule	rat/mouse	IgG2b	PS/2	CRL-1911
Intercellular adhesion molecule 1, mouse	rat	IgG2b	YN1/1.7.4	CRL-1878
Intercellular adhesion molecule 1, mouse	rat/mouse	IgG2a	BE29G1	HB-233
Interferon gamma receptor, mouse	rat/mouse	IgA; kappa	GR-96	CRL-2013
Interferon gamma receptor, mouse	rat/mouse	IgG2a; kappa	GR-20	CRL-2024
Interferon, gamma, human	mouse	IgG1	γ3-11.1	HB-8700†
Interferon, gamma, human	mouse	IgG1	IFGCP-F1BA10	HB-8291†
Interferon, gamma, mouse	rat/mouse	IgG1	R4-6A2	HB-170
Interleukin 1 beta, human	mouse	IgG1; kappa	ILB1-H21	HB-10220†
Interleukin 1 beta, human	mouse	IgG1; kappa	ILB1-H34	HB-10221†
Interleukin 1 beta, human	mouse	IgG1; kappa	ILB1-H6	HB-10219†
Interleukin 1 beta, human	mouse	IgG2b; kappa	ILB1-H67	HB-10222†
Interleukin 1 beta, recombinant, bovine	mouse	IgG1	SA22	CRL-2052
Interleukin 15, human	mouse	IgG1	hIL-15-M110	HB-12061†
Interleukin 15, human	mouse	IgG1	hIL-15-M111	HB-12062†
Interleukin 2 receptor, human	mouse	IgG1	2A3A1H	HB-8555†
Interleukin 2 receptor, human	mouse	IgG2a	7G7B6	HB-8784†
Interleukin 2 receptor, mouse	rat/mouse	IgM; kappa	7D4	CRL-1698
Interleukin 2 receptor, mouse	rat/mouse	IgG1	PC 61 5.3	TIB-222
Interleukin 2, mouse	rat/mouse	IgG2a	S4B6-1	HB-10968†
Interleukin 8 receptor type B (IL-8R-B), human	mouse	IgG2a	10H2.12.1	HB-11494†
Interleukin 8 receptor type B (IL-8R-B), human	mouse	IgG2a	4D1.5.7	HB-11495†
Interleukin 8, human	mouse	IgG1	EL-NC-1S	HB-9647†
Interleukin 8 (IL-8), human	mouse	IgG2a	A5.12.14	HB-11553†
Interleukin 8 (IL-8), rabbit	mouse	IgG2a	6G4.2.5	HB-11722†
Intermediate filaments	mouse	IgG1	α Intermediate Filament	TIB-131
Intracellular adhesion molecule 1 (ICAM-1), canine	mouse	IgG1	CL18/6	CRL-2518
Intracellular adhesion molecule 1 (ICAM-1), human	mouse	IgG2a	R6.5.D6.E9.B2	HB-9580†
Intracellular adhesion molecule 1 (ICAM-1), mouse	rat	IgG2b	YN1/1.7.4	CRL-1878
Intracellular adhesion molecule 1 (ICAM-1), mouse	rat/mouse	IgG2a	BE29G1	HB-233
Intracellular adhesion molecule 1 (ICAM-1), rat	mouse	IgG1	127H	HB-11911†
Invected protein, *Drosophila melanogaster*	mouse	IgG1	4D9D4	CRL-1818
J5 endotoxin core, *Escherichia coli*	mouse	IgG1	J5-1	HB-8297†
J5 endotoxin core, *Escherichia coli*	mouse	IgG1	J5-2	HB-8298†
K99 pilus, *Escherichia coli*	mouse	IgG1; kappa	2BD4E4 K99	HB-8178†
Kappa light chain (monotypic determinant), rat	mouse	IgG2b	RG7/9.1 HLK	TIB-169
Kappa light chain (RI-1a and RI-1b allotypes), rat	mouse	IgG2a; kappa	MAR 18.5	TIB-216
Kappa light chain [kappa 1b (LEW)], rat	mouse	IgG2a	RG7/7.6 HL	TIB-172
Kappa light chain, human	mouse	IgG1; kappa	141PF11	HB-45
Kappa light chain, human	mouse	IgG1	HP6053	CRL-1758
Kappa light chain, human	mouse	IgG1; kappa	TB 28-2	HB-61
Kappa light chain, mouse	rat/mouse	IgG1	187.1	HB-58
Kidney tubules, human	mouse	IgG1	DAL K20	CRL-2288
Kidney tubules, human	mouse	IgG1	DAL K29	CRL-2291
Kininogen heavy chain, human	mouse	IgG1	2B5	HB-8963†
Kininogen light chain, human	mouse	IgG1	C11C1	HB-8964†
Kunitz soybean trypsin inhibitor	mouse	IgG1; kappa	C129	HB-9516†
Kunitz soybean trypsin inhibitor	mouse	IgG1; kappa	C171	HB-9515†
Kunitz soybean trypsin inhibitor	mouse	IgG1; kappa	C180	HB-9517†
L d, D b and D q	mouse	IgG2a; kappa	28-14-8S	HB-27
L d, D q, L q and L b	mouse	IgG2a; kappa	30-5-7S	HB-31
L3T4 antigen (T cell), mouse	rat/mouse	IgG2b	GK1.5	TIB-207
La Crosse Virus, G1 envelope glycoprotein	mouse	IgG2b	807.15	CRL-2287
La Crosse Virus, G1 envelope glycoprotein	mouse	IgG1	807.31	CRL-2282
La Crosse Virus, G1 envelope glycoprotein	mouse	IgG2a	807.33	CRL-2290
La/SSB, bovine	mouse	IgG	La1	HB-8609†
LAM-1, human	mouse	IgG1	DREG200	HB-302
LAM-1, human	mouse	IgG1	DREG56	HB-300
Lambda 1 light chain, mouse	mouse	IgG1; kappa	LS-136	TIB-157
Lambda light chain, human	mouse	IgG2a	HP6054	CRL-1763

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Laminin	rat/mouse	IgG2b	2AB1-IA10	HB-8210†
LECAM, human	mouse	IgG1	DREG200	HB-302
LECAM, human	mouse	IgG1	DREG56	HB-300
Legionella pneumophila	mouse	IgG2a	LP3IIG2	HB-8472†
Legionella pneumophila serogroup 1	mouse	IgG3	Lp1 MAB 1	CRL-1765
Legionella pneumophila serogroup 1	mouse	IgG2b	Lp1 MAB 2	CRL-1770
Legionella pneumophila serogroup 1	mouse	IgG2b	Lp1 MAB 3	CRL-1767
Leptomeningeal cell, rat neural antigen-2, RAN-2)	mouse	IgG2a	Ran-2	TIB-119
Leptospira pomona type kennewicki	mouse	IgA	2D7F10	CRL-2025
Leu 200 glycoproteins, human	mouse	IgG2a; kappa	4C	HB-8311†
Leu-5	mouse	IgM	TM1	HB-169
Leu8, human	mouse	IgG1	DREG200	HB-302
Leu8, human	mouse	IgG1	DREG56	HB-300
Leu8, mouse	rat/mouse	IgG2a	MEL-14	HB-132
Leukocyte common antigen, human	mouse	IgG2a; kappa	GAP 8.3	HB-12
Leukocyte function antigen 1, alpha subunit, mouse	rat/mouse	IgG2a; kappa	M17/4.4.11.9 (new clone of M17/4.2)	TIB-217
Leukocyte function antigen 1, mouse	rat/mouse	IgG2b	FD441.8	TIB-213
LEW RT1.A	rat/mouse	IgM	WFL3C6.1	HB-8157†
LEW RT1.A	rat/mouse	IgM	WFL4F12.3	HB-8156†
Lewis a and b blood group antigens, human	mouse	IgG3	151-5-G2-12	HB-8322†
Lewis a and b blood group antigens, human	mouse	IgG3	151-5-G3-5	HB-8323†
Lewis a antigen	mouse	IgG1	BC9-E5	CRL-1670
Lewis a antigen	mouse	IgG2a; kappa	CA3-F4	CRL-1667
Lewis a antigen	mouse	IgG1; kappa	CF4-C4	CRL-1716
Lewis a blood group antigen, human	mouse	IgG3	151-6-A7-9	HB-8324†
Lewis b blood group antigen, human	mouse	IgG1	130-3-F7-5	HB-8326†
Lewis b blood group antigen, human	mouse	IgM	143-2-A6-11	HB-8325†
Lex (tumor-associated fucoganglioside)	mouse	IgM	FHCR-1-2624/FH6/ FHOT-1-3019	HB-8873†
LFA-1, beta subunit, mouse	rat/mouse	IgG2a; kappa	M18/2.a.12.7 (new clone of M18/2.a.8)	TIB-218
LFA-1, mouse	rat/mouse	IgG2b	FD441.8	TIB-213
LFA-1, mouse	rat/mouse	IgG2a; kappa	M17/4.4.11.9 (new clone of M17/4.2)	TIB-217
LFA-1, mouse	rat/mouse	IgG2b; kappa	M17/5.2	TIB-237
LGL-1	rat/mouse	IgG2a	4D11	HB-240
Lgp100a	rat/mouse	IgG2a	30-C7	TIB-106
Lipopolysaccharide, chlamydia	mouse	IgG3	L2I-6	HB-8705†
Lipoprotein H2, *Pseudomonas aeruginosa*	mouse	IgG1	MA1-6	CRL-1783
Lipoprotein receptor related protein (LRP), 515-kDa subunit, rabbit	mouse	IgG1	IgG-5D7	CRL-1938
Lipoprotein receptor related protein (LRP), 85-kDa subunit, rabbit	mouse	IgG1	IgG-1B3	CRL-1937
Lipoprotein receptor related protein (LRP), carboxy terminal	mouse	IgG1	IgG-11H4	CRL-1936
Low density lipoprotein (LDL) receptor, bovine	mouse	IgG1	9D9	CRL-1703
Low density lipoprotein (LDL) receptor, bovine	mouse	IgG2b	C7	CRL-1691
Low density lipoprotein (LDL) receptor, human	mouse	IgG1	IgG-4A4	CRL-1898
Low density lipoprotein (LDL), human	mouse	IgG1	B1B3	CRL-2249
Low density lipoprotein (LDL), human	mouse	IgG1	B1B6	CRL-2248
LPAM-1, mouse	rat/mouse	IgG2b	R1-2	HB-227
Lung cancer	mouse	IgG1	L18	HB-8628†
Lung cancer	mouse	IgM	L5	HB-8627†
Lung cancer, human	mouse	IgG2a; kappa	703D4	HB-8301†
Luteinizing hormone (hLH) beta core fragment, human	mouse	IgG1 (kappa)	B505	HB-12000†
Luteinizing hormone releasing hormone (LHRH), carboxy terminal	mouse	IgG1	USASK/DSIL-LHRH-A1	HB-9094†
Luteinizing hormone/chorionic gonadotropin (LH/hCG) receptor, human	mouse	IgG2a	FSHR-323	CRL-2689

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Luteinizing hormone/chorionic gonadotropin (LH/hCG) receptor, human	mouse	IgG1	LHR-1055	CRL-2687
Luteinizing hormone/chorionic gonadotropin (LH/hCG) receptor, human	mouse	IgG1	LHR-29	CRL-2685
Luteinizing hormone/chorionic gonadotropin (LH/hCG) receptor, human	mouse	IgG1	LHR-74	CRL-2686
Ly 6.2C, mouse	mouse	IgG1	143-4.2	CRL-1970
Lyb 2.1, mouse	mouse	IgG2b	10-1.D.2	TIB-165
Lyb 8.2, mouse	mouse	IgG1	Cy34.1.2	TIB-163
Lymphocyte function antigen 1 (LFA-1) alpha subunit, human	mouse	IgG1	TS1/22.1.1.13	HB-202
Lymphocyte function antigen 1 (LFA-1) beta subunit, human	mouse	IgG1	TS1/18.1.2.11	HB-203
Lymphocyte function antigen 1 (LFA-1), human	mouse	IgG1	TS2/4.1.1	HB-244
Lymphocyte function antigen 1, mouse	rat/mouse	IgG2b; kappa	M17/5.2	TIB-237
Lymphocyte function antigen 2 (LFA-2), human	mouse	IgG1	TS2/18.1.1	HB-195
Lymphocyte function antigen 3 (LFA-3), human	mouse	IgG1	TS2/9.1.4.3	HB-205
Lymphocyte Peyer's patch HEV adhesion molecule, mouse	rat/mouse	IgG2b	R1-2	HB-227
Lymphocyte surface receptor for endothelium, mouse	rat/mouse	IgG2a	MEL-14	HB-132
Lymphocyte, mouse	rat/mouse	IgM	GL7	HB-254
Lymphoma cells, canine	mouse	IgG2a	Hybridoma 231	HB-9401†
Lymphoma cells, canine	mouse	IgG1	Hybridoma 234	HB-9402†
Lymphoma cells, canine	mouse	IgG2a	Hybridoma 234 s.2a	HB-9403†
Lyt 2.2, mouse	mouse	IgM	83-12-5	CRL-1971
Lyt-1 (all alleles), mouse	rat/mouse	IgG2a	53-7.313	TIB-104
Lyt-2 (all alleles), mouse	rat/mouse	IgM	3.155	TIB-211
Lyt-2 (all alleles), mouse	rat/mouse	IgG2a	53-6.72	TIB-105
Lyt-2.1, mouse	mouse	IgG2a	116-13.1	HB-129
Lyt-2.2, mouse	mouse	IgM	41-3.48	HB-130
Lyt-2.2, mouse	mouse	IgM	HO-2.2	TIB-150
Lyt-2.2, mouse	rat/mouse	IgG2b	2.43	TIB-210
Mac-1, alpha chain, mouse	rat/mouse	IgG2b	M1/70.15.11.5.HL	TIB-128
Mac-1, beta subunit, mouse	rat/mouse	IgG2a; kappa	M18/2.a.12.7 (new clone of M18/2.a.8)	TIB-218
Mac-1, human	mouse	IgG1	LM2/1.6.11	HB-204
Mac-2, mouse	rat/mouse	IgG2a; kappa	M3/38.1.2.8 HL.2	TIB-166
Mac-3 (mouse macrophage antigen, 110-kDa glycoprotein)	rat/mouse	IgG1; kappa	M3/84.6.34	TIB-168
Macrophage, activated, mouse	rat/mouse	IgG2a	158.2	HB-8466†
Macrophage, human	mouse	IgG1; kappa	14E5	HB-174
Macrophage, mouse	rat/mouse	IgG2b	F4/80	HB-198
Macrophage, mouse	rat/mouse	IgG2b	M1/70.15.11.5.HL	TIB-128
Macrophage, mouse	rat/mouse	IgG2a; kappa	M3/38.1.2.8 HL.2	TIB-166
Macrophage, pig	mouse	IgG1; kappa	74-22-15	HB-142
Macrophage, pig	mouse	IgG2b; kappa	74-22-15A	HB-142.1
Macrophage, pig	mouse	IgM; kappa	76-5-28	HB-153
Macrophage, pig	mouse	IgM; kappa	76-6-7	HB-141
MAdCAM-1, mouse	rat/mouse	IgG2a	MECA-367	HB-9478†
MAdCAM-1, mouse	rat/mouse	IgG2a	MECA-89	HB-292
Malignant cultured cells, human	mouse	IgM	B5 NIH	HB-10569†
Mammalian H-Y antigen	mouse	IgM; kappa	HY3-11.27	HB-8116
Mammalian sperm acrosomal vesicle	mouse	IgG1	HS-21 (subclone 1H3)	HB-255
Mammalian splicing factor (SC35)	mouse	IgG1	anti-SC35	CRL-2031
Mammary carcinoma cell line, human	mouse		UCD/AB 6.01	HB-8693†
Mammary carcinoma cell line, human	mouse		UCD/AB 6.11	HB-8458†
Mammary tumor cell cytoplasmic antigen, human	mouse	IgG1	3B18	HB-8654†
Mammary tumor cells, human	mouse	IgM	B25.2	HB-8107†
Mammary tumor cells, human	mouse	IgG1	B38.1	HB-8110†

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Mammary tumor cells, human	mouse	IgG1	B6.2	HB-8106†
Mammary tumor cells, human	mouse	IgG1	B72.3	HB-8108†
Medullary thymic epithelium, mouse	rat/mouse	IgM	MD2	HB-229
Melanoma associated antigens, human	mouse	IgG	WI-MN-1	HB-8672†
Melanoma cell line, human (M-1 antigen system)	mouse	IgG1	LI 27	HB-8437†
Melanoma cell line, human (M-11 antigen system)	mouse	IgG2a	AL 1-27	HB-8441†
Melanoma cell line, human (M-12 antigen system)	mouse	IgG1	LI 66	HB-8442†
Melanoma cell line, human (M-13 antigen system)	mouse	IgG1	E 20	HB-8443†
Melanoma cell line, human (M-16 antigen system)	mouse	IgM	K 114	HB-8444†
Melanoma cell line, human (M-18 antigen system)	mouse	IgG3	R_{24}	HB-8445†
Melanoma cell line, human (M-19 antigen system)	mouse	IgG1	L235	HB-8446†
Melanoma cell line, human (M-20 antigen system)	mouse	IgG2a	L101	HB-8447†
Melanoma cell line, human (M-23 antigen system)	mouse	IgG1; kappa	L230	HB-8448†
Melanoma cell line, human (M-26 antigen system)	mouse	IgG1	A123	HB-8451†
Melanoma cell line, human (M-27 antigen system)	mouse	IgM	A124	HB-8452†
Melanoma cell line, human (M-28 antigen system)	mouse	IgG2a	B5	HB-8453†
Melanoma tumor-specific antigen, human	mouse	IgG2a	XMMME-001	HB-8759†
Melanoma tumor-specific antigen, human	mouse	IgG2a	XMMME-002	HB-8760†
Mesothelial and ciliated cell protein, 130 kDa, human and rat	mouse	IgM; kappa	anti-130-kDa Mesothelial-Ciliated Cells	CRL-2401
Microglobulin, beta-2, human	mouse	IgG2b	BBM.1	HB-28
Microglobulin, beta-2, human	mouse	IgG1; kappa	L368	HB-149
Microglobulin, beta-2, rat	mouse	IgG1	4C9	CRL-2437
Monocyte Fc receptor (high affinity, FcRI), human	mouse	IgG1	32.2	HB-9469†
Monocyte, human	mouse	IgG2b	3C10	TIB-228
Monocyte, human	mouse	IgG2a; kappa	4F2C13	HB-22
Monocyte, human	mouse	IgG1	63D3	HB-44
Monocyte, human	mouse	IgM; kappa	MMA	HB-78
Monocyte-derived neutrophil chemotactic factor, human	mouse	IgG1	EL-NC-1S	HB-9647†
Mononuclear cells, human	mouse	IgG2b	OKM 1	CRL-8026
MOPC167 idiotype (V kappa 24)	rat/mouse	IgG1 and IgG2a	28-6-20	CRL-2489
Mu heavy chain, human	mouse	IgG1; kappa	DA4-4	HB-57
Mu heavy chain, mouse	rat/mouse	IgG2b	331.12	TIB-129
Multidrug resistance protein (MRP)	mouse	IgG1	QCRL-1	HB-11765†
Multidrug resistance protein (MRP)	mouse	IgG2a	QCRL-3	HB-11766†
Muscle, heart	mouse	IgG2a; kappa	356-1	HB-181
myb (c-*myb*), chicken	mouse	IgG2b	MYB 2-3.76	CRL-1728
myb (c-*myb*), chicken	mouse	IgG2b	MYB 2-37.63	CRL-1726
myb (c-*myb*), chicken	mouse	IgG1	MYB 2-7.77	CRL-1724
myb (v-*myb*)	mouse	IgG2b	MYB 2-3.76	CRL-1728
myb (v-*myb*)	mouse	IgG2b	MYB 2-37.63	CRL-1726
myb (v-*myb*)	mouse	IgG1	MYB 2-7.77	CRL-1724
myc (c-*myc*) protein, human	mouse	IgG1	MYC 1-9E10.2	CRL-1729
myc (c-*myc*) protein, human	mouse	IgG1	MYC CT 14-G4.3	CRL-1727
myc (c-*myc*) protein, human	mouse	IgG1	MYC CT 9-B7.3	CRL-1725
Myeloid cell antigen, human	mouse	IgG1; kappa	Anti-My-10 clone 28/8/8/14/4	HB-8483†
Myeloid leukemia (CD33), human	mouse	IgG2a	M195	HB-10306†
Myocardium	mouse	IgG2a; kappa	356-1	HB-181
Myosin heavy chain, adult, human	mouse	IgG2a	A4.1025	CRL-2044
Myosin heavy chain, adult, slow, human and rodent	mouse	IgM	A4.840	CRL-2043
Myosin heavy chain, cardiac alpha, rat	mouse	IgG2b	BA-G5	HB-276
Myosin heavy chain, embryonic, human and rodent	mouse	IgG1	F1.652	CRL-2039
Myosin heavy chain, embryonic, rat	mouse	IgG1	BF-45	HB-278
Myosin heavy chain, embryonic, rat	mouse	IgG1	BF-86	HB-279
Myosin heavy chain, fast IIa, human and rodent	mouse	IgG1	N2.261	CRL-2047
Myosin heavy chain, fast IIa, rodent	mouse	IgG1	A4.74	CRL-2041
Myosin heavy chain, fast IIa, rodent	mouse	IgM	N1.551	CRL-2040
Myosin heavy chain, fast, human	mouse	IgG1	A4.74	CRL-2041
Myosin heavy chain, neonatal and adult fast, human	mouse	IgM	N3.36	CRL-2042

* Part of the NBL collection; see page 12. † Patent item; see page 12.
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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
Myosin heavy chain, slow, human and rodent	mouse	IgG1	A4.951	CRL-2046
Myosin heavy chain, slow, human and rodent	mouse	IgG1	N2.261	CRL-2047
Myosin heavy chain, type 1, rat	mouse	IgG1	BA-D5	HB-287
Myosin heavy chain, type 2A, rat	mouse	IgG1	SC-71	HB-277
Myosin heavy chain, type 2B, rat	mouse	IgM	BF-F3	HB-283
NAP-1 (neutrophil attractant/activation protein 1)	mouse	IgG1	EL-NC-1S	HB-9647†
Nerve growth factor (NGF) receptor, primate	mouse	IgG1	200-3-G6-4 (20.4)	HB-8737†
Neuroblastoma, human	mouse	IgM	PI 153/3	TIB-198
Neutrophil attractant/activation protein 1, human	mouse	IgG1	EL-NC-1S	HB-9647†
Neutrophils, mouse	rat/mouse	IgM	J11d.2	TIB-183
nG4m(b) isoallotope, human	mouse	IgG1	HP6016	CRL-1787
Nicotinic acetylcholine receptor, *Torpedo californica*	mouse	IgG1	88B	CRL-1967
NK cell antigen, mouse (LGL-1)	rat/mouse	IgG2a	4D11	HB-240
NK cell target ligand on NC-37 cells	mouse	IgM	18C2.8.3	HB-9571†
NK cell target ligand on NC-37 cells	mouse	IgM	7C6.5.4	HB-9574†
NK cells, human	mouse	IgM; kappa	HNK-1	TIB-200
NK cells, mouse	mouse	IgG2a	PK136	HB-191
Non-small cell lung carcinoma (NSCLC), human	mouse	IgG1	L18	HB-8628†
Non-small cell lung carcinoma (NSCLC), human	mouse	IgM	L5	HB-8627†
O-antigen, *Escherichia coli* O157	mouse	IgM	MARC 29F8	CRL-2508
O-antigen, *Escherichia coli* O157	mouse	IgM	MARC S5	CRL-2507
OKT-10 like molecule, human	mouse	IgG1	THB-7	HB-136
o-Phosphotyrosine	mouse	IgG1; kappa	2G8.D6	HB-8190†
Ornithine decarboxylase (ODC), mouse	mouse	IgM	B11	HB-8372†
Ovarian carcinoma cell line (2774), human	mouse	IgG1	ME195	HB-8431†
Ovarian carcinoma cell line (2774), human	mouse	IgG2a	MF 116	HB-8411†
Ovarian carcinoma cell lines, human	mouse	IgM	MH55	HB-8412†
Ovarian carcinoma, human	mouse	IgG2a; IgG2b	OVB-3	HB-9147†
Oxysterol binding protein	mouse	IgG2a	IgG-B16	CRL-1899
Oxysterol binding protein (OSBP), rabbit	mouse	IgG1	IgG-11H9	CRL-2213
Oxytocin-neurophysin (NP-OT), rat	mouse	IgG2b; kappa	PS 38	CRL-1950
Oxytocin-neurophysin (NP-OT), rat	mouse	IgG2b; kappa	PS 60	CRL-1800
Oxytocin-neurophysin (NP-OT), rat	mouse	IgG2a; kappa	PS 67	CRL-1797
p12 *gag* protein of murine leukemia viruses (MuLV)	mouse	IgG2b	548	CRL-1890
p15 *gag* protein of murine leukemia viruses (MuLV)	mouse	IgG2b	34	CRL-1889
p15E *env* protein of murine leukemia viruses (MuLV)	mouse	IgG3	372	CRL-1893
p30 *gag* protein of murine leukemia virus (MuLV)	rat/mouse	IgG1	R187	CRL-1912
Parainfluenzavirus type 3, fusion glycoprotein (F), human	mouse	IgG1	9-4-3	HB-8935†
Parainfluenzavirus type 3, hemagglutinin (HN), human	mouse	IgG2a	13-5-9-6-2	HB-8934†
Paramyosin, *Schistosoma mansoni*	mouse	IgG2a	MBL-Sm-1A6	HB-194
Paramyosin, *Schistosoma mansoni*	mouse	IgG2a	MBL-Sm-4B1	HB-193
Pasturella multocida type D dermonecrotic toxin	mouse	IgG1	1B2A3	CRL-1965
PDGF B, v-*sis* form	mouse	IgG2a	116	HB-9367†
PDGF B, v-*sis* form	mouse	IgG2b	232	HB-9372†
PDGF B, v-*sis* form	mouse	IgG1	52	HB-9361†
Peptidoglycan, bacterial	mouse	IgG3; kappa	15B2	HB-8510†
Peptidoglycan, bacterial	mouse	IgG1; kappa	3C11	HB-8511†
Peptidoglycan, bacterial	mouse	IgM; kappa	3F6	HB-8512†
Peptidoglycan, bacterial	mouse	IgM; lambda	3G3	HB-8516†
Periostin	mouse	IgG1; kappa	5H8	CRL-2646
PETA-3 (CD151)	mouse	IgG1	41-2	CRL-2695
PETA-3 (CD151)	mouse	IgG1	50-6	CRL-2696
Peyer's patch endothelial cells, human	mouse	IgG2a	Hermes-3	HB-9480†
Peyer's patch endothelial cells, mouse	rat/mouse	IgG2a	MECA-367	HB-9478†
P-glycoprotein, human	mouse	IgG2b	443-17F9-1C6	CRL-2694
Pgp-1 glycoprotein, mouse	rat/mouse	IgG2b	IM7.8.1	TIB-235
Pgp-1, mouse	rat/mouse	IgG1	KM114	TIB-242
Pgp-1, mouse	rat/mouse	IgG1	KM201	TIB-240
Pgp-1, mouse	rat/mouse	IgG2a	KM703	CRL-1896

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
Pgp-1, mouse	rat/mouse	IgG2a	KM81	TIB-241
Phenylarsonate	mouse	IgE	SE-1.3	HB-137
Phosphatidylinositol 4-kinase, type II, bovine	mouse	IgG1; kappa	4C5G	CRL-2538
Phosphotyrosine	mouse	IgG1; kappa	2G8.D6	HB-8190†
Phosphotyrosine	mouse	IgG3; kappa	FB2	CRL-1891
Phosphotyrosine	mouse	IgG1	P-tyr-1	CRL-1955
Plasmodium falciparum merozoite antigen	mouse	IgG2b	MAb 5.2	HB-9148
Platelet glycoprotein GPIIIa, human	mouse	IgG1; kappa	LK-4	CRL-2345
Platelet-derived growth factor B chain (PDGF B, v-*sis* form)	mouse	IgG2a	116	HB-9367†
Platelet-derived growth factor B chain (PDGF B, v-*sis* form)	mouse	IgG2b	232	HB-9372†
Platelet-derived growth factor B chain (PDGF B, v-*sis* form)	mouse	IgG1	52	HB-9361†
Platelets, human	mouse	IgG1	7E3	HB-8832†
p-nitroanaline amide derivatives	mouse	IgG1	P3 6D4 (SCRF 43.1)	HB-9168†
p-nitroanaline amide derivatives	mouse	IgG1	P3 8D2 (SCRF 43.1)	HB-9169†
p-nitroanaline amide derivatives	mouse	IgG1	QPN1 12C9 (SCRF 43.2)	HB-9500†
p-nitroanaline amide derivatives	mouse	IgG1	QPN1 22F5 (SCRF 43.2)	HB-9509†
Polypeptide, synthetic	mouse	IgM	7C8	HB-8465†
Polypeptide, synthetic, Asp-Tyr-Lys-Asp-Asp-Asp-Asp-Lys	mouse	IgG2b	4E11	HB-9259†
Polypyrimidine tract binding protein (PTB)	mouse	IgG2b; kappa	mAb BB7	CRL-2501
Pig parvovirus (PPV)	mouse	IgG1	3C9-D11-H11	CRL-1745
Primate tissue, normal	mouse	IgM	B5 NIH	HB-10569†
Prostate antigen (PA), human	mouse	IgM; kappa	F5-A-1/22.8.13	HB-8051†
Prostate antigen (PA), human	mouse	IgG1	RLSD06	HB-8527†
Prostate antigen (PA), human	mouse	IgG1	RLSD09	HB-8525†
Prostate cancer antigen, human	mouse	IgG1	7E11C5	HB-10494†
Prostate cancer, human	mouse	IgG3	P25.48	HB-9119†
Prostate epithelial cells	mouse/mouse	IgG1	Prost 410	HB-11426†
Prothrombin, abnormal, human	mouse	IgG1	JO1-1	HB-8638†
P-selectin, human	mouse	IgG1	WAPS 12.2	HB-299
Pseudomonas aeruginosa (flagella type b)	human		20H11	CRL-9300†
Pseudomonas aeruginosa lipopolysaccharide (LPS) Fisher immunotype 1 (IATS type 6)	human	IgM	C5B7	CRL-8753†
Pseudomonas aeruginosa lipopolysaccharide (LPS) Fisher immunotype 4 (IATS type 1)	human	IgM	9D10	CRL-8752†
Pseudomonas aeruginosa lipopolysaccharide (LPS) Fisher immunotype 7	human	IgM	8E7	CRL-8795†
Pseudorabies virus (PRV)	mouse	IgG2b	3G9F3	CRL-1843
Pseudorabies virus (PRV)	mouse	IgG2b	6D8MB4	CRL-1842
Qa-1b, mouse	mouse	IgG1 (kappa)	4C2.4A7.5H11	CRL-2744
Qa-1b, mouse	mouse	IgG1 (kappa)	6A8.6F10.1A6	CRL-2743
RAN-2 (rat neural antigen-2)	mouse	IgG2a	Ran-2	TIB-119
ras (c-*ras*) protein, p21	rat	IgG2a	Y13-238	CRL-1741
ras (c-*ras*) protein, p21	rat	IgG1	Y13-259	CRL-1742
ras (v-*ras* K) oncogene peptide, synthetic	mouse	IgG1 and IgG2b	147-67C6	CRL-2654
ras (v-*ras*) protein, p21	rat	IgG2a	Y13-238	CRL-1741
ras (v-*ras*) protein, p21	rat	IgG1	Y13-259	CRL-1742
ras oncogene peptide, synthetic	mouse	IgG1; kappa	146-03E04	CRL-2650
ras, H/N, peptide, synthetic	mouse	IgG1; kappa	142-24E5	CRL-2649
ras, Ha, p21	mouse	IgG1	MX	HB-9158†
Rat neural antigen-2 (RAN-2)	mouse	IgG2a	RAN-2	TIB-119
Receptor, 1,25-dihydroxy vitamin D3, pig	mouse	IgG1	XVI E6E6G10	HB-9496†
Receptor, acetylcholine, neuronal, chicken	rat/mouse	IgG2a	mAb 270	HB-189
Receptor, acetylcholine, neuronal, rat	rat/mouse	IgG2a	mAb 270	HB-189
Receptor, CD28, mouse	hamster/mouse	IgG	PV1	HB-12352†
Receptor, complement, type 3 (CR3), mouse	rat/mouse	IgG2b	5C6 Clone 1	CRL-1969
Receptor, Coxsackievirus-adenovirus, human	mouse	IgG1	RmcB	CRL-2379
Receptor, epidermal growth factor (EGF)	mouse	IgG1	225	HB-8508†

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
Receptor, epidermal growth factor (EGF)	mouse	IgG1	455	HB-8507†
Receptor, epidermal growth factor (EGF)	mouse	IgG2a	528	HB-8509†
Receptor, epidermal growth factor (EGF)	mouse	IgG	579	HB-8506†
Receptor, epidermal growth factor (EGF), human	mouse	IgG2a; kappa	Mab 108	HB-9764†
Receptor, epidermal growth factor (EGF), human	mouse	IgM	Mab 96	HB-9763†
Receptor, Epstein-Barr virus (EBV)	mouse	IgG2a; kappa	THB-5	HB-135
Receptor, Fc alpha, human	mouse	IgM	My 43.51	HB-12128†
Receptor, follicle stimulating hormone (FSH), human	mouse	IgG1	FSHR-18	CRL-2688
Receptor, insulin, human	mouse	IgG1; kappa	αIR-1	HB-175
Receptor, insulin, placental, human	mouse	IgG1	DII 33.1	CRL-1827
Receptor, interferon gamma, mouse	rat/mouse	IgG2a; kappa	GR-20	CRL-2024
Receptor, interferon gamma, mouse	rat/mouse	IgA; kappa	GR-96	CRL-2013
Receptor, interleukin 12 (IL-12), beta 1 subunit, human	rat/mouse	IgG2a	HIL12R1.2B10	CRL-2359
Receptor, interleukin 2 (IL-2), human	mouse	IgG1	2A3A1H	HB-8555†
Receptor, interleukin 2 (IL-2), human	mouse	IgG2a	7G7B6	HB-8784†
Receptor, interleukin 2 (IL-2), mouse	rat/mouse	IgM; kappa	7D4	CRL-1698
Receptor, interleukin 2 (IL-2), mouse	rat/mouse	IgG1	PC 61 5.3	TIB-222
Receptor, interleukin 8, type B, human	mouse	IgG2a	10H2.12.1	HB-11494†
Receptor, interleukin 8, type B, human	mouse	IgG2a	4D1.5.7	HB-11495†
Receptor, luteinizing hormone/chorionic gonadotropic (LH/hCG), human	mouse	IgG2a	FSHR-323	CRL-2689
Receptor, luteinizing hormone/chorionic gonadotropic (LH/hCG), human	mouse	IgG1	LHR-1055	CRL-2687
Receptor, luteinizing hormone/chorionic gonadotropic (LH/hCG), human	mouse	IgG1	LHR-29	CRL-2685
Receptor, luteinizing hormone/chorionic gonadotropic (LH/hCG), human	mouse	IgG1	LHR-74	CRL-2686
Receptor, nerve growth factor (NGF), primate	mouse	IgG1	200-3-G6-4 (20.4)	HB-8737†
Receptor, stem cell factor (SCF), human	mouse	IgG2a	BA7.3C.9	HB-10716†
Receptor, transferrin, human	mouse	IgG2a	L5.1	HB-84
Receptor, transferrin, human	mouse	IgG1	OKT 9	CRL-8021
Receptor, transferrin, mouse	rat/mouse	IgM	R17 208.2	TIB-220
Receptor, transferrin, mouse	rat/mouse	IgG2a	R17 217.1.3	TIB-219
Receptor, vascular endothelial growth factor (VEGF), mouse	rat/mouse	IgG1; kappa	DC101	HB-11534†
Receptor, very low density lipoprotein (VLDL)	mouse	IgG1	IgG-6A6	CRL-2197
Receptor, vitonectin, human	mouse	IgG1	B6H12.2	HB-9771†
Red blood cells, sheep	mouse	IgM; lambda	N-S.2.1	TIB-108
Red blood cells, sheep	mouse	IgM; kappa	N-S.4.1	TIB-110
Red blood cells, sheep	mouse	IgG3; kappa	N-S.7	TIB-114
Red blood cells, sheep	mouse	IgG2b	N-S.8.1	TIB-109
Red blood cells, sheep	mouse	IgG2a; kappa	S-S.1	TIB-111
Red blood cells, sheep	mouse	IgM; kappa	S-S.3	TIB-112
Renal carcinoma cell lines, human	mouse	IgG1	ME195	HB-8431†
Renal carcinoma cell lines, human	mouse	IgG2a	MF 116	HB-8411†
Renal cell carcinoma, human	mouse	IgG1	DAL K20	CRL-2288
Renal cell carcinoma, human	mouse	IgG1	DAL K29	CRL-2291
Renal cell carcinoma, human	mouse	IgG1	DAL K45	CRL-2292
Renin, hog	mouse	IgG1	F32 VIII C4	CRL-1653
Reovirus type 3, sigma 1 hemagglutinin	mouse	IgG2a	9BG5	HB-167
REP-1, human	mouse	IgG1	IgG-2F1	CRL-2419
Retinal Muller cell, rat	mouse	IgG2a	RAN-2	TIB-119
Retinoblastoma, human	mouse	IgM	PI 153/3	TIB-198
Ricin, A chain (A1 and A2)	mouse	IgG1	TFTA1	CRL-1771
Ricin, B chain	mouse	IgG1	TFTB1	CRL-1759
RNA-DNA hybrids	mouse	IgG	S9.6	HB-8730†
Saccharide antigen, Gal beta1-3GalNAc (T antigen)	mouse	IgG3; kappa	JAA-F11	CRL-2381
Saxitoxin binding component of electroplex membrane	mouse	IgG1	VD-10	HB-68
Sca-1, mouse	rat/mouse	IgG2a	E13 161-7	HB-215

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
SCAP	mouse	IgG2b	IgG-9D5	CRL-2347
Schistosoma mansoni surface (cercariae) glycoprotein	mouse	IgA	129A3/1	HB-8087†
Schistosoma mansoni surface (cercariae) glycoprotein	mouse	IgG1	130C3/2B/8	HB-8088†
Schistosoma mansoni surface (cercariae) glycoprotein	mouse	IgG1	132C4A/4	HB-8086†
L-Selectin, human	mouse	IgG1	DREG200	HB-302
L-Selectin, human	mouse	IgG1	DREG56	HB-300
L-Selectin, mouse	rat/mouse	IgG2a	MEL-14	HB-132
L-Selectin, sheep and bovine	mouse	IgG1	DU1-29	HB-263
Sex lethal gene product (Sxl), female specific, *Drosophila melanogaster*	mouse	IgG1	mSXL 104	CRL-1953
Sex lethal gene product (Sxl), female specific, *Drosophila melanogaster*	mouse	IgG1	mSXL 114	CRL-1954
Sex lethal gene product (Sxl), female specific, *Drosophila melanogaster*	mouse	IgG1	mSXL 18	CRL-1952
Sex lethal gene product (Sxl), female specific, *Drosophila melanogaster*	mouse	IgG1	mSXL 5	CRL-1951
Shiga toxin	mouse	IgG1; kappa	13C4	CRL-1794
Shiga-like toxin I (SLTI)	mouse	IgG1; kappa	13C4	CRL-1794
Shiga-like toxin II (SLT-II)	mouse	IgG1; kappa	11E10	CRL-1907
Shiga-like toxin II (SLT-II)	mouse	IgG2a; kappa	11F11	CRL-1908
SLA a, c, d	mouse	IgG2a	7-34-1	CRL-1945
SLA ABd (pig histocompatibility antigen)	mouse	IgG2b; kappa	74-11-10	HB-139
SR proteins (pre-mRNA splicing factors)	mouse	IgG1	anti-SR (1H4)	CRL-2383
SR proteins (pre-mRNA splicing factors)	mouse	IgM	MAb104	CRL-2067
SR proteins, conserved epitope	mouse	IgG1	16H3	CRL-2385
src (v-*src*) oncogene peptide, synthetic	mouse	IgG1	201-45E9	CRL-2670
src (v-*src*) oncogene peptide, synthetic	mouse	IgG2a; IgG2b	203-7D10	CRL-2651
src/yes oncogene peptide, synthetic	mouse	IgG1	202-11A8	CRL-2669
SREBP cleavage activating protein	mouse	IgG2b	IgG-9D5	CRL-2347
SREBP-2, hamster	mouse	IgG2b	IgG-7D4	CRL-2198
SRp20 proteins (pre-mRNA splicing factors)	mouse	IgG1	anti-SRp20 (7B4)	CRL-2384
Stem cell antigen 1, mouse (Sca-1)	rat/mouse	IgG2a	E13 161-7	HB-215
Stem cell factor (SCF) receptor, human	mouse	IgG2a	BA7.3C.9	HB-10716†
Stem cells, mesenchymal, human	mouse	IgG1	SH2	HB-10743†
Stem cells, mesenchymal, human	mouse	IgG2b	SH3	HB-10744†
Stem cells, mesenchymal, human	mouse	IgG1	SH4	HB-10745†
Sterol regulatory element binding protein (dSREBP), *Drosophila melanogaster*	mouse	IgG1; kappa	IgG-3B2	CRL-2693
Sterol regulatory element binding protein (SREBP), human	mouse	IgG1	IgG-2A4	CRL-2121
Sterol regulatory element binding protein 2 (SREBP-2), hamster	mouse	IgG2b	IgG-7D4	CRL-2198
Sterol regulatory element binding protein 2 (SREBP-2), human	mouse	IgG1	IgG-1C6	CRL-2224
Sterol regulatory element binding protein 2 (SREBP-2), human	mouse	IgG1; kappa	IgG-1D2	CRL-2545
Streptococcus mutans	mouse	IgG2a; kappa	SWLA1	HB-12559†
Streptococcus mutans	mouse	IgG2a; kappa	SWLA2	HB-12560†
Streptococcus mutans	mouse		SWLA3	HB-12558†
Surface membranes of cancer cells	mouse	IgG1 (kappa)	IMM002.69.47.4	CRL-13007†
SV40 T antigen	mouse	IgG2a	PAb 101	TIB-117
SV40 T antigen	mouse	IgG1	PAb 100	TIB-115
SV40 T antigen, N terminal	mouse	IgG2a	PAb 108	TIB-230
SV40 T antigen, N terminal	mouse	IgG2a	PAb 108	TIB-230
Swine leucocyte antigen (SLA)	mouse	IgG2a	7-34-1	CRL-1945
T antigen, N terminal, SV40	mouse	IgG2a	PAb 108	TIB-230
T antigen, non-viral (NVT), mouse	mouse	IgG2b	PAb 122	TIB-116
T antigen, SV40	mouse	IgG2a	PAb 101	TIB-117

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
T antigen, SV40	mouse	IgG1	PAb 100	TIB-115
T cell (activated), human	mouse	IgG1	10D2F6	HB-11103†
T cell (activated), human	mouse	IgG1	OKT 9	CRL-8021
T cell antigen receptor (Jurkat cells), human	mouse	IgM; kappa	C305	CRL-2424
T cell antigen receptor, gamma/delta negative, sheep	mouse	IgG1; kappa	86D	HB-286
T cell antigen receptor, human, major framework determinant	mouse	IgG1	(BF1) 8A3.31	HB-9283†
T cell antigen receptor, human, major framework determinant	mouse	IgG2a	W4F.5B	HB-9282†
T cell antigen receptor, mouse	hamster/mouse	IgG	H57-597	HB-218
T cell antigen receptor, mouse	rat/mouse	IgG2b	TR 310	HB-219
T cell precursor, human	mouse	IgG1	OKT 10	CRL-8022†
T cell receptor	mouse	IgG1	1G12	CRL-2827
T cell receptor, gamma/delta, mouse	hamster/mouse	IgG	UC3-10A6	CRL-1988
T cell receptor, gamma/delta, mouse	hamster/mouse	IgG	UC7-13D5	CRL-1989
T cells, cytotoxic, pig	mouse	IgG2a; kappa	76-2-11	HB-143
T cells, cytotoxic/suppressor, human	mouse	IgG1	OKT 5	CRL-8013†
T cells, cytotoxic/suppressor, human	mouse	IgG1	OKT 5	CRL-8016†
T cells, cytotoxic/suppressor, human	mouse	IgG2a	OKT 8	CRL-8014
T cells, gamma/delta positive, bovine	mouse	IgG1	IL-A29	CRL-1874
T cells, helper/inducer, human	mouse	IgG2b	OKT 4	CRL-8002†
T cells, helper/inducer, mouse	rat/mouse	IgG2b	GK1.5	TIB-207
T cells, human	mouse	IgM	2T8-3E10	HB-8213†
T cells, human	mouse	IgM	3Pt12B8	HB-8136†
T cells, human	mouse	IgG1; kappa	5E9C11	HB-21
T cells, human	mouse	IgG1	OKT 1	CRL-8000†
T cells, human	mouse	IgG1	OKT 11	CRL-8027†
T cells, human	mouse	IgG2a	OKT 3	CRL-8001†
T cells, human	mouse	IgG1; kappa	T3-3A1	HB-2
T cells, mouse	mouse	IgM; kappa	20-10-5S	HB-23
T cells, pig	mouse	IgM; kappa	76-5-28	HB-153
T cells, pig	mouse	IgM; kappa	76-6-7	HB-141
T cells, rabbit	mouse	IgM	9AE10	CRL-1761
T cells, rabbit	mouse	IgG1	L11/135	TIB-188
T12 (120 kDa) antigen, human T cells	mouse	IgM	3Pt12B8	HB-8136†
T15 idiotype	mouse	IgG1; kappa	AB1-2	HB-33
TAG-72 (tumor-associated glycoprotein), human	mouse	IgG1; kappa	CC 49	HB-9459†
T-B activating molecule (T-BAM), human	mouse	IgG2a	5c8	HB-10916†
Tetanus toxin	human/mouse	IgG1	9F12	HB-8177†
Tetanus toxoid	human	IgG; kappa	SA13	HB-8501†
TGF-beta-2, mouse	mouse	IgG1	1D11.16.8	HB-9849†
Theophylline	mouse	IgG1; kappa	17/14	HB-8153†
Theophylline	mouse	IgG1; kappa	30/15	HB-8152†
Theophylline	mouse	IgG1; kappa	61/7	HB-8154†
Thy-1 antigen, human	mouse	IgG1	K117	HB-8553†
Thy-1 antigen, mouse	mouse	IgM	HO-22-1	TIB-100
Thy-1 antigen, mouse	rat/mouse	IgG2a	M5/49.4.1	TIB-238
Thy-1.1 antigen, mouse	mouse	IgM	T11D7e2	TIB-103
Thy-1.2 antigen, mouse	mouse	IgM	HO-13-4	TIB-99
Thy-1.2 antigen, mouse	rat/mouse	IgG2b	30-H12	TIB-107
Thy-1.2 antigen, mouse	rat/mouse	IgM	J1j.10	TIB-184
Thymic lymphocyte, human	mouse	IgG1	OKT 6	CRL-8020†
Thymocyte (E rosette positive), human	mouse	IgG1	OKT 11	CRL-8027†
Thymocyte, human	mouse	IgG2a	A1G3	HB-177
Thymocyte, human	mouse	IgG1	OKT 6	CRL-8020†
Thymocytes, rabbit	mouse	IgM	9AE10	CRL-1761
Thymus, cortical epithelium, human	mouse	IgG2b	CDR2	HB-214
Thymus, cortical epithelium, human	mouse	IgG2	TE3	HB-209
Thymus, cortical epithelium, human	mouse	IgM	TE4	HB-207
Thymus, epithelium, human	mouse	IgM	TE15	HB-206
Thymus, epithelium, human	mouse	IgG1	TE16	HB-210

* Part of the NBL collection; see page 12. † Patent item; see page 12.
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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
Thymus, epithelium, human	mouse	IgM	TE19	HB-211
Thymus, epithelium, human	mouse	IgG2a	TE8	HB-212
Thymus, human	mouse	IgG1	TE7	HB-208
Thyroid stimulating hormone (TSH) receptor alpha subunit, human	mouse	IgG1	TSHR-R5T-44	CRL-2681
Thyroid stimulating hormone (TSH) receptor alpha subunit, human	mouse	IgG1	TSHR-T5-51	CRL-2680
Thyroid stimulating hormone (TSH) receptor alpha subunit, human	mouse	IgG1	TSHR-T5U-317	CRL-2682
Thyroid stimulating hormone (TSH) receptor beta subunit, human	mouse	IgG1	TSHR-R5T-34	CRL-2683
Thyroid stimulating hormone (TSH) receptor beta subunit, human	mouse	IgG2a	TSHR-T3-365	CRL-2684
L-Thyroxine (T4, 3,5,3',5'-tetraiodo-L-thyronine)	mouse	IgG1	T4 Clone 5 (10-0101, 0062-83)	HB-8500†
Ti1b antigen, human	mouse	IgM	2T8-3E10	HB-8213†
TL antigen, mouse	mouse	IgG2a	I(TL.m9)	HB-131
TL antigen, mouse	rat/mouse	IgG2a	HD168	HB-252
Transferrin receptor, human	mouse	IgG2a	L5.1	HB-84
Transferrin receptor, human	mouse	IgG1	OKT 9	CRL-8021
Transferrin receptor, mouse	rat/mouse	IgM	R17 208.2	TIB-220
Transferrin receptor, mouse	rat/mouse	IgG2a	R17 217.1.3	TIB-219
Transforming growth factor-beta2, mouse	mouse	IgG1	1D11.16.8	HB-9849†
Treponema pallidum	mouse	IgM	1939-3G5	HB-8133†
Treponema pallidum	mouse	IgG1	1939-8G2	HB-8134†
Trichinella spiralis	mouse	IgM	$7C_2C_5C_{12}$	HB-8678†
Trifucosylated type 2 chain glycolipids	mouse	IgM	FHCR-1-2075/FH5	HB-8770†
2,4,6-Trinitrophenyl (TNP)	mouse	IgG1	1B7.11	TIB-191
2,4,6-Trinitrophenyl (TNP)	mouse	IgA	2F.11.15	TIB-194
2,4,6-Trinitrophenyl (TNP)	mouse	IgE (Iga haplotype)	IGEL a2	TIB-142
2,4,6-Trinitrophenyl (TNP)	mouse	IgE (Igb haplotype)	IGEL b4	TIB-141
Trop-1, human	mouse	IgG2a	162-21.2	HB-241
Trop-2, human	mouse	IgG1 (Igh-4a allotype)	162-46.2	HB-187
Trophoblasts, human	mouse	IgG1 (Igh-4a allotype)	162-46.2	HB-187
Tubulin, beta, nematode	mouse	IgG	P3D	HB-11129†
Tumor, intracellular antigen, human	human/mouse	IgM	Ch13	HB-8573†
Tumor, intracellular antigen, human	human/mouse	IgM	Gr431	HB-8575†
Tumor, intracellular antigen, human	human/mouse	IgM	Te39	HB-8577†
Tumor-associated glycoprotein (TAG-72), human	mouse	IgG1 kappa	CC 49	HB-9459†
Tumors, human	mouse	IgM	B5 NIH	HB-10569†
Tumors, neuroectoderm, human	mouse	IgM	PI 153/3	TIB-198
Uracil DNA glycosylase (UDG), human	mouse	IgM	37.04.12	HB-9312†
Uracil DNA glycosylase (UDG), human	mouse	IgG	40.10.09	HB-9311†
Uracil DNA glycosylase (UDG), human	mouse	IgM	42.08.07	HB-9313†
Uterine carcinoma cell lines, human	mouse	IgM	MH55	HB-8412†
VacA (vacuolating cytotoxin)	mouse	IgG1; kappa	5E4	CRL-2635
VacA (vacuolating cytotoxin)	mouse	IgG1; kappa	5G5	CRL-2633
VacA (vacuolating cytotoxin)	mouse	IgG1; kappa	B3D	CRL-2634
Vascular cell adhesion molecule 1, human and macaque	mouse	IgG1; kappa	VIII-6G10	HB-10519†
Vascular cell adhesion molecule 1, mouse	rat/mouse	IgG1; kappa	M/K-1.9	CRL-1910
Vascular cell adhesion molecule 1, mouse	rat/mouse	IgG1; kappa	M/K-2.7	CRL-1909
Vascular endothelial growth factor (VEGF) receptor-2, mouse	rat/mouse	IgG1; kappa	DC101	HB-11534†
Vasopressin-neurophysin (NP-AVP), rat	mouse	IgG2b; kappa	PS 41	CRL-1799
Vasopressin-neurophysin (NP-AVP), rat	mouse	IgG2b; kappa	PS 45	CRL-1798
VCAM-1, human and macaque	mouse	IgG1; kappa	VIII-6G10	HB-10519†
VCAM-1, mouse	rat/mouse	IgG1; kappa	M/K-1.9	CRL-1910
VCAM-1, mouse	rat/mouse	IgG1; kappa	M/K-2.7	CRL-1909

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Hybridomas by Antigenic Determinant

Antigenic Determinant	Species of Hybridoma	Isotype	Name	ATCC® No.
VEGF receptor 1	mouse	IgG1 (kappa)	6.12	CRL-13006†
Very late antigen 1 (VLA-1) alpha, human	mouse	IgG1	TS2/7.1.1	HB-245
Very late antigen 1 (VLA-1) beta, human	mouse	IgG1	TS2/16.2.1	HB-243
Very late antigen 4 (VLA-4), mouse	rat/mouse	IgG2b	R1-2	HB-227
Very late antigen 4 (VLA-4), sheep	mouse	IgG2b	FW3-218-1	HB-261
Very low density lipoprotein (VLDL) receptor	mouse	IgG1	IgG-6A6	CRL-2197
Vesicular stomatitis virus surface glycoprotein	mouse	IgG1	I1-Hybridoma	CRL-2700
v-fms oncogene peptide (synthetic)	mouse	IgG1 and 2b (kappa)	290-4E10	CRL-2662
Vitamin B6	mouse	IgG1	E6(2)2	HB-8172†
Vitamin D3 receptor, pig	mouse	IgG1	XVI E6E6G10	HB-9496†
Vitonectin receptor (VnR), human	mouse	IgG1	B6H12.2	HB-9771†
Vulva, cancer	human	IgG4	VLN3G2	HB-8636†
Vulva, cancer	human	IgG	VLN6H2	HB-8633†
WC1, bovine	mouse	IgG2a	CC15	HB-265
WC1, bovine	mouse	IgG1	CC39	HB-274
WC1, bovine	mouse	IgG1	IL-A29	CRL-1874
WC3 bovine B cell antigen (BoWC3)	mouse	IgG1	CC21	HB-288
WC4, bovine	mouse	IgG1	CC55	HB-282
WC4, bovine	mouse	IgG1	CC57	HB-268
Yellow fever virus	mouse	IgG2a; kappa	2D12	CRL-1689
Yersinia pestis, F1 antigen	mouse	IgA	F1-3G8-1	HB-192
yes (c-*yes*) oncogene peptide, synthetic	mouse	IgG1	240-13D10	CRL-2672
Zonae pellucidae 1 (ZP1), human	mouse	IgG1 (kappa)	H1.6	CRL-2567
ZP1 glycoprotein, mouse	rat/mouse	IgG2a	M1.4	CRL-2464
ZP2 glycoprotein, human	mouse	IgG1; kappa	H2.8	CRL-2568
ZP2 glycoprotein, mouse	rat/mouse	IgG2a	IE-3	CRL-2463
ZP3 glycoprotein, human	mouse	IgG1; kappa	H3.1	CRL-2569
ZP3 glycoprotein, mouse	rat/mouse	IgG2a	IE-10	CRL-2462

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